

RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

EDITOR

Howard P. Doub, M.D.
Detroit, Michigan



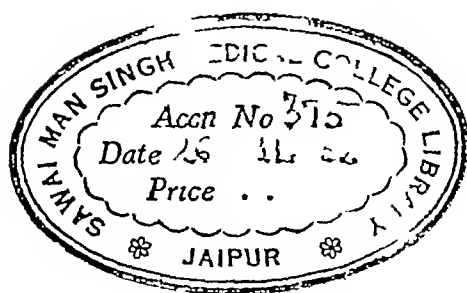
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No 1

The Pathology of Rheumatic Diseases¹

D MURRAY ANGEVINE, M D

Madison, Wis

THIS DESCRIPTION of pathology of joints, tendons, and bursae has been prepared as a preliminary to a discussion of irradiation therapy in certain diseases of these structures. Accordingly the subject will be treated in its broadest aspects, with special stress on pathogenesis. It should be emphasized that such an elucidation is greatly hampered by our almost complete lack of knowledge of etiology. An entirely satisfactory or accurate classification cannot be given on a pathological basis without some consideration of etiology. The criteria for diagnoses of most rheumatic diseases are primarily clinical, with secondary consideration being given to the pathological lesions. As our knowledge of this comparatively neglected group of diseases increases, it is probable that more attention will be given to this phase of the subject. In the description to follow, rheumatic fever and tuberculosis will not be considered in any detail.

NORMAL ANATOMY

While it is not the purpose of this paper to discuss anatomy at any great length, certain significant features of structures to be mentioned subsequently will be described. We are primarily concerned with (a) the synovial membrane and villi of joints, the synovial lining of tendons and bursae, and (b) the articular hyaline car-

tilage. The former structure, namely synovial membrane, is of great importance and is the tissue primarily involved in most of these diseases, whereas the cartilage is highly important in degenerative joint disease or osteoarthritis.

The inner lining of the articular capsule, or *synovial membrane*, is smooth, glistening, and of a gray-yellow color. It is reflected over tendons that pass through joint spaces and ceases at the margins of the articular cartilages. It is composed of thin, delicate connective tissue and covered on its free surface by a layer of mesothelium. In certain joints, especially the knee, there are numerous foldings or reduplications of this membrane which are not considered as true synovial villi. Synovial villi are observed with difficulty by the unaided eye. If a joint be opened and submerged under water or saline, the villi float and are readily seen. They are usually slightly polypoid, being narrower at the point of attachment, they frequently branch and are most numerous in the region of the perichondrium, where synovial membrane and cartilage meet. There is a rich capillary network over the entire surface that is easily seen with slight magnification.

Articular cartilage is composed of cartilage cells enmeshed in a fibrillary matrix. The superficial cells are flattened and

¹ From the Department of Pathology, University of Wisconsin Medical School, Madison, Wis. Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

parallel to the surface, whereas the deeper ones are oval and arranged in vertical rows so that there is a tendency to split in a vertical direction

CLASSIFICATION

A most satisfactory and desirable classification of joint diseases at present is that of the American Rheumatism Association, an abbreviated form of which follows

Acute Infections of Known Etiology
Staphylococcus, Streptococcus, Gonococcus, Meningococcus, etc

Chronic Infections of Known Etiology
Syphilis
Tuberculosis

Probably Infectious (Etiology Not Known)

Rheumatic fever

Rheumatoid arthritis (proliferative or atrophic)

Marie-Strümpell spondylitis

Still's disease

Degenerative Joint Disease or Osteoarthritis

It seems essential that in so far as possible the clinician, roentgenologist, and pathologist should use a similar terminology not only for this group but for all diseases. As roentgen studies and laboratory procedures come into wider and more universal use, the necessity for common terminologies and similar classifications is increasingly evident. Considerable progress in this direction was made during the war, when specialists from numerous localities were brought together, subjects discussed, and ideas exchanged.

ACUTE INFECTIONS OF KNOWN ETIOLOGY

When organisms such as the gonococcus, meningococcus, or one of the pyogenic bacteria lodge in a joint, they are usually carried by the blood stream from an infectious process elsewhere. There is frequently an increase in synovial fluid, the cytology of which reflects closely the type of inflammatory exudate in the synovial membrane. Observations on experimental arthritis in animals at various time inter-

vals give a clear indication of the sequence of events. Such lesions can be readily produced by intravenous injections of hemolytic streptococci or other organisms. (1) The first gross evidence of inflammation is a dilatation of vessels of the synovial membrane. On microscopic examination the villi are edematous and there is a moderate infiltration of the synovial tissue with polymorphonuclear leukocytes and lymphocytes, depending upon the virulence and number of the infecting organisms. Such a lesion may subside and heal, become purulent and produce a pyoarthrosis with destruction of cartilage, or may follow a comparatively chronic course from the time of onset.

From other experimental observations (2) it is believed that the anatomic structure of the synovial villus is a significant factor in localizing microorganisms in joints.

It is evident that in clinical cases the degree of involvement of the joint may vary considerably in different infections, depending upon the number and virulence of the infecting organisms. In the final analysis, the diagnosis depends upon the isolation of the etiologic agent from the synovial tissue or fluid.

CHRONIC INFECTIONS OF KNOWN ETIOLOGY

Tuberculosis is the most important of the chronic infections of known etiology. It usually involves the synovial membrane, and the extensive degenerative changes in cartilage are secondary to extensive pannus formation. Syphilitic arthritis is a rarity if it does occur.

PROBABLY INFECTIOUS (ETIOLOGY UNKNOWN)

Rheumatic Fever In rheumatic fever the joints are involved for relatively brief periods, effusion, if present, rapidly subsides, usually leaving no residual. The inflammation in the synovial membrane is granulomatous and characterized by degeneration of collagenous tissue and a monocyctic infiltration. Subcutaneous nodules appear about joints and at sites of pressure, certain histological similarities

to those of rheumatoid arthritis have been observed (3) The histopathology of subcutaneous nodules from both diseases has been described in detail by Bennett, Zeller, and Bauer (4)

Rheumatoid Arthritis This disease most frequently involves the small joints of the hands, then spreads centripetally to the larger joints Involvement is frequently bilaterally symmetrical but not necessarily so The first observable change is a periarticular soft-tissue fusiform swelling, usually of the midphalangeal joints of the fingers This is caused largely by inflammation and edema of the synovial membrane and subsynovial tissues, which become thickened There is frequently effusion into the joint space, and aspirated fluid often contains large numbers of polymorphonuclear leukocytes The lesion may subside and recur or may be progressive, in which instance the membrane is greatly thickened and the villi are enlarged, both are extensively infiltrated with large numbers of cells, chiefly lymphocytes, plasma cells, and monocytes Many of the lymphocytes are arranged in foci, especially in the villi The lining synovial cells are frequently several layers thick and occasionally covered by fibrinoid material The walls of many medium-sized arteries in the subsynovial tissues are thickened and there is endothelial proliferation that narrows the lumen As one seldom if ever has an opportunity to observe these vessels early in the disease, it is difficult to evaluate the significance of these alterations It appears most probable that they are secondary to the inflammatory process in the synovial membrane, where many of the small arterioles frequently show hyalinization This histologic picture is consistent with a clinical diagnosis of rheumatoid arthritis but will not establish the diagnosis

The next significant change is a proliferation of the fibrous connective tissue in the region of the perichondrium This vascular fibrous tissue, known as a pannus, grows over the surface of the articular cartilage and interferes with its normal

nutrition, resulting in subsequent degenerative changes When the pannus proliferates extensively, it fuses with the pannus on the opposite articulating surface to produce a fibrous ankylosis While these changes are taking place in the joint proper, certain important alterations occur elsewhere The muscles about the joint atrophy from disuse There is also atrophy of the bone trabeculae in the ends of the bones adjacent to affected joints One occasionally observes, also, a fibrosis, as well as a chronic inflammatory cellular exudate, in the intertrabecular spaces adjacent to the articular surfaces

Subcutaneous nodules, usually periarticular, are frequently observed in this disease Their chief characteristics are areas of fibrinoid degeneration surrounded by monocyctic cells arranged in a palisade fashion Attention has recently been focused on rather widespread inflammatory changes involving peripheral nerves (5) and voluntary muscles (6) Baggenstoss and Rosenberg (7) have also described changes in the heart which they attribute to rheumatoid arthritis These observations are of considerable interest and require more extensive investigation They indicate that this disease is widely disseminated and, although joint involvement is apparently the primary lesion, it is entirely possible that it may be only one important manifestation of a widespread process

Marie-Strumpell Spondylitis This disease is considered by most authorities to be a form of rheumatoid arthritis of the spine, involving the axial in contrast to the appendicular skeleton The fact that it almost exclusively affects young male adults seems to indicate that it is a different disease, however, further clarification of this point must depend on information yet to be obtained The initial involvement is an inflammation of the synovial membrane of the costovertebral articulations, and there is a similar involvement of the sacroiliac joints As the disease progresses, there is an ankylosis of these joints that explains the symptoms and signs

Studies of the early pathological changes are not available and probably will not be because of the nature of the disease. Biopsy material from the involved joints would be of considerable value and interest.

Still's Disease This is a disease of children that is also considered as a form of rheumatoid arthritis (8),¹¹ at least until additional adequate evidence is obtained to warrant a further separation from this group. The important features are lymph node enlargement, usually of the cervical, axillary, and inguinal groups. Microscopic examination of the enlarged nodes reveals hyperplasia. There is usually splenic enlargement, frequently due to amyloid infiltration. Fibrinous and fibrous pleurisy and pericarditis are common. The heart is often enlarged and verrucae have been described on the tricuspid and pulmonary valves. The usual lesion in the joints is a fusiform swelling progressing to deformity. Early in the course there are pain, swelling, and stiffness of the joints. As the disease progresses, the hands present a picture very similar to that characteristic of rheumatoid arthritis in adults, that is, flexion of the proximal phalangeal joints. Hyperextension of the distal phalanges is an important feature. Histologic sections show proliferation of synovial cells and an extensive chronic inflammation throughout the synovial membrane. The blood vessels are numerous, thin-walled and dilated in the early cases. Deformities appear relatively early in children and are usually accompanied by extensive demineralization of bone.

DEGENERATIVE JOINT DISEASE

The term degenerative joint disease has been advocated by Bauer and Bennett (9) in preference to osteoarthritis, and is more desirable. The disease is initially one of degeneration of cartilage. Several important factors may influence the onset. The most important seems to be wear and tear over and above what is normal for any given joint. The vascular supply about the margin of articular cartilage

also gradually decreases with increasing age.

The first observable alteration in the cartilage is a slight flaking of the superficial layer, this is followed by fibrillation, which is a fraying or separation of the fibrillary tissue surrounding the cartilage cells. The cartilage cells show varying degrees of degeneration, and the articular cartilage stains irregularly due to deposition of mineral salts. As the lesion progresses, there is loss of cartilage, extending to the underlying bone in severe cases. When this occurs, there is a thickening of the underlying bone, which becomes smooth and very hard, like ivory, known as eburnation. There is some regeneration of cartilage, mostly at the periphery, this is possible because of the relatively rich vascular supply of the perichondrium. Rarefaction of bony trabeculae occurs when the disease is painful enough to cause disuse. Localized areas of rarefaction of bone have been variously attributed to islands of cartilage or to local osteoclastic resorption. It seems entirely possible that this may bear some relationship to alteration in the vascular supply of the bone. Osteophytes may arise from perichondrium and also from the fibrous tissue of the periosteum. Herberden's nodes that appear on the base of the terminal phalanges of the fingers are periosteal or tendon osteophytes arising in the extensor tendon at its point of attachment to the periosteum. They may become calcified or ossified. Changes in the synovial membrane are limited and may undergo hyperplasia and fibrosis due to mechanical irritation. Small cartilaginous nodules may form in synovial villi and give rise to loose bodies or joint mice.

ACUTE AND CHRONIC BURSITIS AND TENOSYNOVITIS

The lining membrane of tendons, tendon sheaths, and bursae is similar histologically to the synovial membrane. It is also fair to assume that it is probably functionally similar. In general, acute inflammation of these structures produces a

picture very similar to that described in the synovial membrane of joints. It is probably caused in most instances by a metastatic infection, trauma, or a combination of both. These structures are occasionally involved in rheumatic fever and rheumatoid arthritis. The chronic inflammatory lesions involving them, chiefly the bursae, probably begin with acute inflammation of the synovial lining, which may subside or continue as a chronic bursitis. Histologically the bursal wall is composed of dense fibrous tissue, the synovial lining composed of villous folds, and infiltrated with cells the character of which depends upon the severity and duration of the lesion. Synovial fluid is often seen between the villi. In chronic bursal lesions one frequently observes calcium deposits in the subsynovial tissue or the fibrous wall.

SUMMARY

The more significant lesions of joints, tendons, and bursae are briefly described, with special emphasis on inflammation of synovial membranes and the subsequent alterations produced by it. A description

of the changes in the cartilage that occur in degenerative joint diseases is also given.

Department of Pathology
University of Wisconsin Medical School
Madison 6 Wis

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SUMARIO

La Patología de las Afecciones Reumáticas

En esta breve reseña de las lesiones más importantes de las articulaciones, tendones y bolsas, recálcase en particular la inflamación de las membranas sinoviales y las alteraciones subsiguientes que la misma provoca. También se presenta una descripción de las alteraciones del cartílago que sobrevienen en la artropatía degenerativa.

En la clasificación de las enfermedades articulares, síguese, en forma abreviada, la de la Asociación Americana del Reumatismo.

Infecciones agudas de Etiología Conocida
Estafilococo, Estreptococo, Gonococo, Meningococo, etc
Infecciones Crónicas de Etiología Conocida
Tuberculosis Sifilis
Probablemente Infección
Reumatismo (Fiebre Reumática)
Artritis Reumatoidea
Espondilitis de Marie-Strümpell
Enfermedad de Still
Artropatía degenerativa (osteoartritis)

Roentgen Diagnostic Aspects of Chronic Arthritis and Bursitis¹

LESTER W PAUL, M.D., and WILLIAM W MOIR, M.D

Madison, Wis

THE PURPOSE of the present communication is to evaluate the place of roentgen examination in the study of chronic joint disease, to correlate the clinical and roentgen aspects, and to demonstrate the pathologic alterations as they are revealed by roentgen study. The entire subject of chronic joint affections is one of such wide scope that it would be impossible to cover it fully in a single paper. Clinically the chronic arthropathies fall into three main groups: (1) chronic joint disease of more or less generalized nature, or at least affecting multiple joints, exemplified by rheumatoid arthritis and degenerative joint disease, (2) chronic arthritis limited to a single or, at the most, a few joints, represented by tuberculous arthritis, neurotrophic arthropathy, traumatic arthritis, gouty arthritis, and the secondary form of degenerative joint disease, (3) chronic disease limited to the periarticular tissues, the most common representative being the so-called subacromial bursitis and the related "frozen shoulder" of the clinician. We shall limit our discussion largely to lesions of the first and third groups, since these constitute the majority of chronic joint and periarticular affections and because, among these, will be found the lesions most amenable to roentgen therapy.

The terminology and classification of arthritis as recommended by the Committee of the American Rheumatism Association will be followed (7). While this is a clinical classification based in so far as possible upon etiology, with its terminology phrased to conform with the *Standard Nomenclature of Disease*, it can be adapted readily to roentgen practice.

It is obvious that roentgen examination is only one phase of the diagnostic study

that patients with chronic joint disease should receive. Solely on a study of the roentgenograms it is not always possible to identify accurately the type of chronic arthritis that a patient may have. As Camp (2) has stated, "the roentgenologist, using only roentgenologic evidence, would have to classify the arthritides as (1) periartthritis, (2) atrophic arthritis, (3) hypertrophic arthritis, and (4) destructive arthritis." These are the fundamental alterations that can be detected in roentgenograms. Yet it would serve no useful purpose for roentgenologists to employ a classification different from that used by their clinical colleagues.

The value of roentgenologic examination in the early stages of chronic arthritis varies with the type of the disease. In rheumatoid arthritis the roentgen findings are not specific, and the early recognition of this disease is largely a clinical problem. The latent period before "characteristic" roentgen changes develop is usually a matter of months or even years. The same is true of the arthritis associated with gout. On the other hand, in degenerative joint disease (osteoarthritis) roentgen examination may reveal well defined changes in a joint which is clinically silent, or nearly so. It follows that a negative roentgenogram is of distinctly more value in excluding degenerative joint disease than it is in ruling out rheumatoid arthritis. In gouty arthritis, roentgenograms may not be diagnostic of the disease for years. The classical text-book picture of large, punched-out defects at the ends of the bones, gross disorganization of joint structure, and lumpy soft-tissue enlargements represents gouty arthritis in an advanced stage, years after its onset (5). The

¹ From the Department of Radiology, University of Wisconsin Medical School and The State of Wisconsin General Hospital, Madison 6, Wis. Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

roentgen pattern of chronic arthritis also is often altered by the natural processes of repair. Thus a rheumatoid arthritic joint may show well marked "hypertrophic" changes if the disease in that particular joint has undergone periodic remissions or quiescence (Fig 1). These factors must

likely to be confused with the bony proliferation which is a feature of degenerative joint disease. "Atrophic arthritis" has been favored by roentgenologists because atrophy is usually the major feature demonstrated on roentgen examination, but it does not cover adequately the patho-



Fig 1 Thirty nine-year old female. Clinical diagnosis rheumatoid arthritis. Roentgenograms show severe involvement of the proximal interphalangeal joints with loss of joint space and pronounced bony proliferation at the proximal joint of the middle finger. In the other fingers the changes are more characteristic of rheumatoid arthritis, with narrowing of joint spaces, erosion of bony articular surfaces and decalcification. The terminal joints are less severely affected.

be kept in mind in any discussion of the roentgen features of chronic arthritis.

RHEUMATOID ARTHRITIS

In the classification mentioned earlier, the term "rheumatoid" is favored over the synonyms "atrophic," "proliferative" and "chronic infectious arthritis." The infectious nature of the disease is considered very probable but remains to be proved. "Proliferative" refers to the pathologic changes in the synovial membrane and is

logical changes which have taken place.

While the clinical pattern of rheumatoid arthritis varies, most cases begin insidiously and run either a protracted and progressive course or undergo remissions of variable length. Eventually the disease leads to more or less crippling deformity of the affected joints. Typically, the peripheral joints are first affected, usually the proximal interphalangeal joints, with a tendency for a symmetrical distribution in the two hands. As the disease progresses,

it affects the more proximal joints, advancing toward the trunk in all extremities, until finally practically every joint in the body may be involved. A curious feature of the disease, for which there is no adequate explanation, is the frequent sparing of the terminal interphalangeal joints. Since the earliest lesions occur in the hands,

may become extremely severe in advanced cases. These changes may be all that can be recognized for months, and in some joints the disease may never progress beyond this stage. Since these roentgen findings are not specific, the roentgenologist can only report periarticular swelling, or at the most periartthritis, even though the

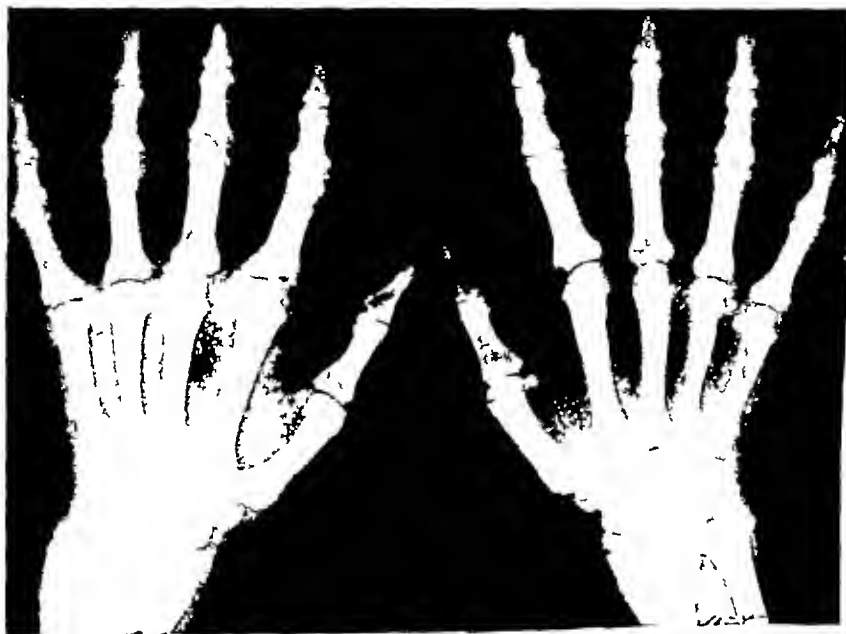


Fig 2 Chronic rheumatoid arthritis of ten years' duration in a fifty two year-old female. The disease began in the proximal interphalangeal joints and later spread to the wrists, elbows, shoulders, ankles, and knees. Roentgenograms of the hands and wrists show many stages of rheumatoid arthritis in the different joints. Some of the proximal interphalangeal joints are beginning to ankylose. The terminal joints are essentially normal.

roentgen examination of these areas should be included in any study of chronic arthritis.

The first roentgen evidence usually is periarticular swelling, characteristically diffuse and fusiform. This is readily demonstrated in the proximal interphalangeal joints. Along with this, or after an interval of several months, decalcification of bone becomes apparent. Although the decalcification is at first limited to the articular ends of the bones near the affected joints, eventually the entire skeleton shows loss of density. This osteoporosis, which is one of the constant features of the disease and is aggravated by bodily disuse,

multiplicity of joints involved, characteristic location, and symmetry of joints affected all point strongly to the diagnosis.

If the disease progresses, destruction of joint cartilage becomes apparent, as shown on the roentgenogram by narrowing of the joint space. This is generally uniform throughout the joint. In some joints, the articular ends of the bones remain smooth until the cartilaginous space completely disappears and bony ankylosis develops. More frequently they show irregular erosion with disappearance of the cortical shadow. This erosion may take the form of small "punched-out" defects. In other joints, it appears as a

fine roughening of the bony surface. All of these variations may be seen in a single hand and wrist (Fig 2). The soft-tissue swelling tends to disappear in the later stages of the disease and is superseded by soft-tissue contractions, which in turn may lead to actual dislocation and severe crippling deformity. If the subluxation is

begin originally in some of the larger joints rather than in the hands, or it may be limited to a few of these large joints. A small percentage of cases show an apparent clinical "cure." Variable amounts of hypertrophic bone reaction may develop as a manifestation of repair, and these hypertrophic features may even-

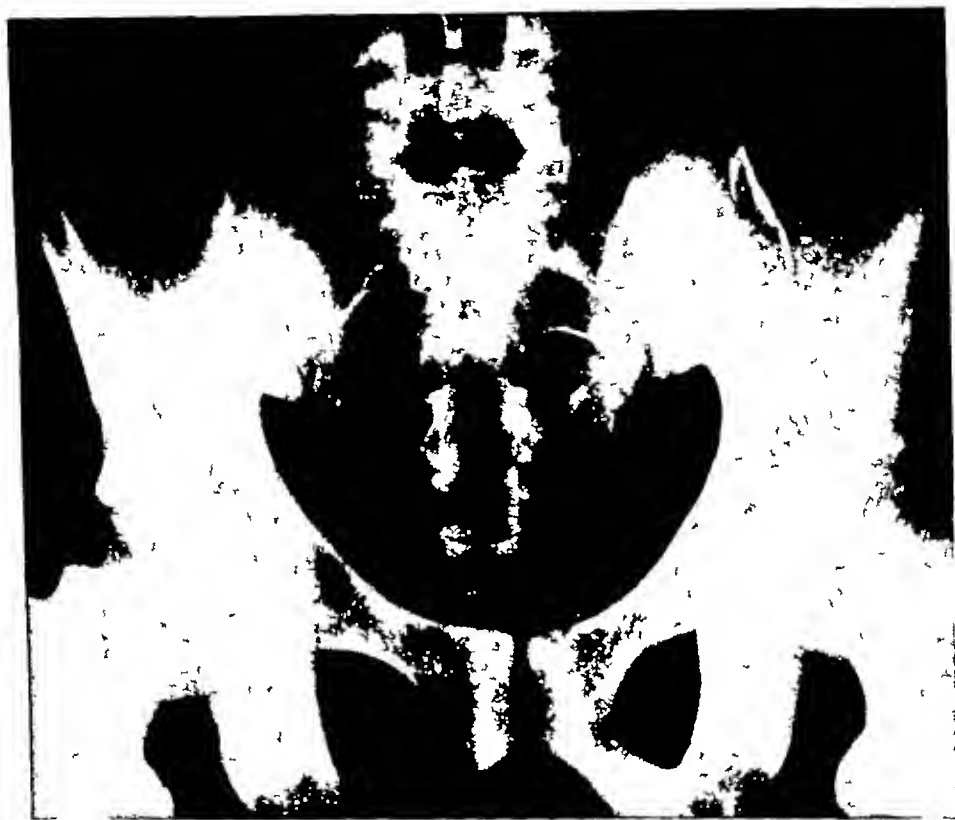


Fig 3 Rheumatoid arthritis of the sacroiliac joints in a twenty-two-year old male who has had intermittent low back pain, worse in damp weather, for the past seven years. The roentgen changes consist of blurred joint spaces, irregular joint margins, and some sclerosis.

pronounced, there is little tendency for bony ankylosis. The disease may become arrested at any stage. If this occurs before much structural change has been produced, the joint may return to a normal or almost normal appearance, the soft-tissue swelling disappearing and the bones regaining a normal density.

This is the usual and well recognized course of rheumatoid arthritis as it affects the peripheral joints. Many cases, however, differ in important respects. The disease may have an acute onset, it may

usually overshadow the atrophic in roentgenograms. Rheumatoid arthritis may also develop in a joint which has previously undergone degenerative changes, especially if the disease begins after middle age. It may be impossible from roentgen study to determine which is the primary disease when both hypertrophic and atrophic alterations are present. Such a lesion is likely to be classified as a "mixed" arthritis.

Rheumatoid Arthritis of the Spine (Marie-Strumpell arthritis, ankylosing arthritis

of the spine, spondylitis rhizomélisque, etc.) The numerous designations applied to this disease attest to the differences of opinion as to its nature and place in the classification of chronic arthritis. The cause is unknown, and while its relationship to rheumatoid arthritis of the peripheral joints is somewhat debatable, many competent investigators believe it should be classified as a form of rheumatoid arthritis (1, 3, 7). Affecting young adult males predominantly, it is one of the common causes of chronic back pain in that age group. The clinical onset is insidious. Roentgen changes may not become apparent until some months or even years after the beginning of symptoms. Characteristically, the earliest roentgen evidence appears in the sacroiliac joints bilaterally (Fig 3). The articular surfaces lose their sharp outlines and the joints have a blurred appearance. Fuzzy sclerosis develops along the joint margins. As the disease advances, the bony margins show gross irregularities, followed in time by ligamentous calcification and finally bony ankylosis. The disease may remain confined to the sacroiliac joints, progressing through all stages, including bony ankylosis. More frequently, there is a slow progression throughout the spine. The facet joints undergo the same changes as occur in the sacroiliacs and finally ankylose. Not all facet joints are involved equally nor at the same time. Concomitantly, calcification in the spinal ligaments begins, and, in progressive cases, continues until a complete shell of calcification surrounds the vertebrae, the end result being the "poker spine" of the clinician. Ligament calcification may, however, be absent or minimal. In later stages, chronic decalcification of bone is a prominent feature.

For demonstrating the early changes, special projections may be necessary. A satisfactory visualization of the sacroiliac joints usually can be obtained by an anteroposterior projection with the roentgen tube angled 25 degrees toward the head. For the lumbar facet joints, oblique views

are necessary. The dorsal facet joints cannot be shown satisfactorily in many cases. The best view of these is obtained with the patient's body rotated slightly off the true lateral.

Still's Disease This disease of children is thought to be identical with rheumatoid arthritis in adults and needs no further discussion here.

DEGENERATIVE JOINT DISEASE

(Degenerative Arthritis, Osteoarthritis, Hypertrophic Arthritis, Osteoarthrosis, etc.)

Although the cause of degenerative joint disease is unknown, it seems well established that infection plays no part. Because of this, many investigators have disliked the use of the term arthritis. "Osteoarthrosis" has been suggested as a better designation. In this country, at least, "osteoarthritis" and "hypertrophic arthritis" seem to be preferred, the latter term being found frequently in the roentgenologic literature because it more aptly describes the changes seen in roentgenograms. "Degenerative joint disease" is given preference in the classification submitted by the Committee of the American Rheumatism Association, but in its discussion the term "osteoarthritis" is used.

When the spine is involved, a variety of descriptive terms have been employed. The joints between the vertebral bodies are not synovial joints and, if the term arthritis is to be limited only to joints covered by synovial membrane, changes occurring along the margins of the vertebral bodies (spurs) and in the intervertebral disks (thinning) cannot rightly be called arthritis. Marginal osteophytes on the vertebral bodies are almost a uniform finding after middle age. Generally these are designated as "hypertrophic changes" rather than "arthritis." In many, but not all, of these patients some degree of thinning of intervertebral disks also is present and the two processes undoubtedly are closely allied. Oppenheimer (6) believes that the marginal spurring is always the result of change in the intervertebral

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For demonstrating the early changes, special projections may be necessary. A satisfactory visualization of the sacroiliac joints usually can be obtained by an anteroposterior projection with the roentgen tube angled 25 degrees toward the head. For the lumbar facet joints, oblique views

are necessary. The dorsal facet joints cannot be shown satisfactorily in many cases. The best view of these is obtained with the patient's body rotated slightly off the true lateral.

Still's Disease This disease of children is thought to be identical with rheumatoid arthritis in adults and needs no further discussion here.

DEGENERATIVE JOINT DISEASE

(Degenerative Arthritis, Osteoarthritis, Hypertrophic Arthritis, Osteoarthrosis, etc.)

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Fig 5 Degenerative joint disease (osteoarthritis) of the fingers in a sixty-year-old female. The terminal joints of the fingers are affected chiefly, particularly of the index finger, which shows well developed Heberden's nodes.
Fig 6 Degenerative joint disease of the hip (osteoarthritis) showing all of the characteristic features of moderately advanced disease



Fig 7 Degenerative arthritis of minimal severity in a fifty-four year-old female with primary complaints referable to the cardiovascular system. Slight narrowing of the medial part of the joint space some increased density of articular surfaces on the inner side small marginal osteophytes, and an irregular fabella
Fig 8 Degenerative joint disease (osteoarthritis) of the knee. In addition to uneven narrowing of the joint space there is a large spur on the anterior tibial articular surface a bony loose body above the patella and fluid in the joint pouch. The fabella is irregular and large.

most often involved. Changes also are relatively common in some of the intertarsal joints, particularly the astragaloscaphoid in patients with flat feet. There is some difference in the roentgen appearances of the disease in the weight-bearing and non-weight-bearing joints. In the fingers the early findings consist of tiny marginal spurs or small calcific flakes along the bases of the distal phalanges.

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These enlarge gradually to form well defined bony protuberances which cause an irregular, knobby thickening, palpable and visible, representing the well known Heberden's nodes, one of the significant clinical diagnostic features of the disease (Fig 5). In more severely affected joints, narrowing of the joint space is present, and the bony articular surfaces become quite irregular. This picture is somewhat



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Fig 9 Degenerative joint disease of the ankle developing secondarily to a congenital clubfoot deformity The changes are similar to those seen in the hip and knee

similar to that seen in rheumatoid arthritis. There are, however, no punched-out defects, and decalcification of the articular ends is not present. Bony trabeculae remain sharp, and a cortical margin may be apparent. The terminal phalanx becomes flexed on the middle, and the finger cannot be completely straightened. Partial subluxations may occur, but bony ankylosis is unusual. In some cases small cystic cavities develop in the ends of the bones, but eburnation of bones seldom is striking.

In the hip, the early signs of this disease vary. In some, the first evidence consists in increased density along the superior acetabular rim. In others, marginal spurring is the earliest feature, but in most cases narrowing of the joint space is the most significant finding. In contrast to rheumatoid arthritis, decrease in joint space in degenerative disease is characterized by its asymmetry and is related closely to the distribution of weight-bearing in the joint (Fig 6). In the hip, this affects the su-

perior portion almost exclusively, since this is the area which receives the thrust of the femoral head in weight-bearing. This narrowing progresses to complete loss of the joint space but without bony ankylosis. This asymmetrical narrowing of the joint space leads to varying degrees of subluxation of the femoral head and, if accompanied by a wearing away of the superior portion of the acetabular fossa, may result in notable deformity. Marginal osteophytes of large size may be present. As the head moves upward in the enlarged acetabular fossa, considerable amounts of calcium may be laid down along the under surface as if to fill more completely the enlarged cavity. The joint surfaces, particularly the acetabular, show increased density, although the bone actually is softer than normal. Cystic appearing cavities develop as sharply outlined rarefactions surrounded by dense sclerotic walls. In some cases the "cysts" appear quite early. Infrequently, degenerative disease in the hip may lead to a general



Fig 10 Degenerative joint disease (osteoarthritis) of the cervical spine in a sixty nine year-old male complaining only of paresthesias in the right ulnar nerve distribution. Lateral roentgenogram shows narrowing of the lower cervical disk spaces, marginal osteophytes and osteoarthritic changes in the facet joints.

deepening and inward bulging of the acetabular cavity, and some cases, at least, of so-called intrapelvic protrusion of the acetabulum seem to be due to this cause.

Degenerative joint disease is the most common chronic joint affection encountered in the knee. In most cases the early changes consist in the development of small spurs along the joint margins, on the tibial spine, along the borders of the intercondylar fossa of the femur, and on the articular edges of the patella. Hypertrophic excrescences may develop on the joint surface of the tibia, particularly at the attachments of the cruciate ligaments. As in the hip, narrowing of the joint space usually appears quite early and may be the first sign (Fig 7). It is generally asymmetrical, with the medial aspect undergoing the most severe change. Increased density of bony articular surfaces also is most pronounced along the

zone of greatest joint-space narrowing. Because of the uneven narrowing of the joint space and the consequent disturbance of weight-bearing alignment, some degree of lateral subluxation of the tibia on the femur is common in advanced lesions, and a varus deformity is frequent. In contrast to the hip, the formation of cystic cavities in the articular ends of the bones is rare. However, a common feature of the disease in this joint, and almost exclusively limited to it, is the development of calcific or bony loose bodies within the joint pouch (Fig 8). The fabella, if present, is enlarged and roughened. Joint effusion is said to be uncommon in this type of disease, but roentgenograms of the knee often show evidence of fluid, and the examination may have been requested to determine the cause of such effusion. In some cases the occurrence of fluid is the chief reason for consulting the physician. It may be that the effusion is due to mechanical irritation from intra-articular loose bodies or to trauma in a joint rendered unstable by the disease.

Unless deformity of the foot is present, degenerative disease in the ankle usually is limited to marginal spurring and some condensation of bone along the articular surfaces. In the presence of stresses and strains due to faulty weight-bearing, the same progression of the disease may occur in the ankle as in the knee and hip (Fig 9).

Degenerative Disease of the Spine The same process that involves the peripheral joints also may affect the spine, but because of anatomical structures peculiar to this region it requires separate discussion. The most common finding, almost universally present in patients above middle age, is hypertrophic spurs along the anterior and lateral margins of the vertebral bodies. These marginal osteophytes are particularly prone to develop in the lower cervical, the lower dorsal, and the lower lumbar areas. When the process begins in younger persons, below the age of fifty, the lower cervical vertebrae often are affected primarily. In addition to the spurs, small calcific or bony deposits

may form in the spinal ligaments, especially the anterior, without any attachment to the adjacent bodies. Bony proliferation along the margins of the spinous processes often is present, as is marginal spurring of the costovertebral joints. In the more severe forms of the disease, some degree of thinning of the intervertebral disks is found (Fig 10). This is particularly likely to occur in the lower cervical region and at the lumbosacral joint, but other disk spaces may be affected. Narrowing of the disk space usually is uniform except

joint space, marginal spurring, increased density of bony articular surfaces, and slight degrees of subluxation, the uppermost facets slipping downward on the ones below. This, combined with the thinning of the adjacent intervertebral disk, may result in distinct narrowing of the corresponding spinal foramina. Marginal spurs are not infrequent on the posterior margins of the vertebrae in the lower cervical and lower lumbar areas. These are more significant from a clinical standpoint than spurs on the other surfaces,



Fig 11 Subacromial bursitis. Amorphous calcified deposit probably in the supraspinatus tendon.

in the dorsal region, where it is most pronounced along the anterior borders. In the presence of scoliosis, these changes are more marked along the concave side of the curvature.

Because this disease is found chiefly in the older age period, senile decalcification of bone usually is present, although the cortical margins of the vertebrae remain distinct and actually may show increased density. Involvement of the facet joints may or may not be present. When it is, the roentgen findings are no different from those seen in other weight-bearing joints, allowing for differences in size of the joints. These changes consist in narrowing of

because of the close association with the spinal nerve roots.

PERIARTICULAR DISEASE

The various forms of periarticular rheumatic disease are of relatively little interest to the roentgenologist, with the exception of lesions about the shoulder, since roentgen findings usually are negative except for periarticular swelling. In the shoulder, periarticular disease is the commonest affection encountered by the clinician. According to Comroe (3), this accounts for 85 to 90 per cent of all complaints in this region. Calcification in the soft tissues about the joint, chiefly the supraspinatus



Fig 12 Contracted shoulder in a fifty year-old female who complained of gradually increasing stiffness of the left shoulder of six months duration. The top roentgenogram shows the shoulder joint with the arm in neutral position. The lower roentgenogram was made with the arm in maximum abduction and internal rotation. Very little motion is demonstrated between the humerus and scapula, the patient being able merely to elevate the shoulder. Usually a third view also is made, with the arm in abduction and external rotation. These three views are useful in the routine study of the shoulder area.

tendon, is found in about 50 per cent of patients suffering from chronic periarthritis of the shoulder (Fig 11). In the remainder, excluding those with post-traumatic residues, such as avulsion of the greater tuberosity of the humerus, the roentgen findings are limited to disuse decalcification of the bones and evidence of soft-tissue contracture of variable degrees. Solely on the basis of roentgen examination it is not possible to determine

whether the calcification is within the bursa or in the tendons. Such calcification can be distinguished from fracture fragments by the homogeneous character of the shadow or shadows and absence of a corresponding defect in the adjacent bone. Special projections may be necessary to demonstrate the calcified deposits. These also are useful in showing the amount of limitation of motion that may be present and serve as an excellent record of such disability when it is desired to follow the results of treatment (Fig 12).

SUMMARY AND CONCLUSIONS

Rheumatoid arthritis and degenerative joint disease (osteoarthritis) account for the majority of chronic disabling joint affections except in the shoulder. In that area, periarticular disease, variously labeled as periarthritis, subdeltoid or subacromial bursitis, chronic adhesive bursitis, etc., is the most common cause of disability.

In early rheumatoid arthritis, roentgen changes usually are limited to periarticular swelling, and this is not specific for the disease. While the clinical course and the associated changes seen in roentgenograms generally follow a fairly characteristic pattern of progression, variations do occur with sufficient frequency to make the diagnosis difficult at times. Characteristically the roentgen changes develop in an orderly manner, beginning with soft-tissue swelling, followed progressively by bone decalcification, narrowing of joint space, erosion of the articular ends of the bones, soft-tissue contractures, and bony ankylosis or gross subluxation. The disease, however, may be arrested at any stage, may progress more rapidly in some joints than in others, or may follow an atypical pattern of joint involvement.

The same variations are encountered in rheumatoid arthritis of the sacroiliac joints and the apophyseal joints of the spine.

Degenerative joint disease (osteoarthritis) often produces well advanced roentgen findings before the onset of clinical complaints. The disease may be

more or less generalized, affecting particularly the terminal interphalangeal joints of the fingers, the spine, and the large weight-bearing joints of the lower extremities. In the spine, the roentgen findings include changes on the vertebral bodies (spurring), in the intervertebral disks (thinning), and in the apophyseal joints. All of these appear to be related processes. In the weight-bearing joints, especially the hip and knee, degenerative disease may develop as a result of long continued stresses due to abnormal weight-bearing. The roentgen changes are similar to those seen in the generalized form of the disease and consist in narrowing of the joint space at the site of greatest weight-bearing thrust, increased density of the articular ends of the bones, marginal osteophyte formation, and cystic rarefactions in the bony articular surfaces or close to them.

In the shoulder, chronic periarticular disease accounts for the majority of disabling affections, the lesion usually being a bursitis, a tendinitis, or both. Calcified deposits in the tendons will be found in

about half of these cases, the others showing only chronic decalcification of the bones and soft-tissue contractures. Calcified deposits also are found in patients without complaints referable to the shoulder, so that visualization of such deposits in roentgenograms does not necessarily indicate an active inflammatory process.

1300 University Ave
Madison Wis

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SUMARIO

Consideraciones sobre el Diagnóstico Roentgenológico de la Artritis y la Bursitis Crónicas

La artritis y la artropatía degenerativa (osteoartritis) reumatoideas comprenden la mayoría de las afecciones incapacitantes crónicas de las articulaciones, si se exceptúa el hombro, en el cual la causa más común de incapacidad radica en alguna afección periarticular, bautizada con los nombres de periartrosis, bursitis subdeltoides o subacromiaca, bursitis adhesiva crónica, etc.

En la artritis reumatoidea temprana las alteraciones roentgenológicas suelen limitarse a edema periarticular, que no es específico para esta dolencia. Si bien la evolución clínica y las alteraciones radiográficas que la acompañan conforman por lo general a un patrón bastante típico de gravación también sobrevienen variaciones con suficiente frecuencia para hacer

a veces difícil el diagnóstico. Característicamente, las alteraciones roentgenológicas aparecen con cierto sistema, comenzando con edema de los tejidos blandos, seguido gradualmente de descalcificación ósea, estrechamiento de los espacios articulares, erosión de los extremos articulares de los huesos, contracturas del tejido blando y anquilosis ósea o subluxación macroscópica. No obstante, la enfermedad puede estacionarse en cualquier etapa, puede avanzar más rápidamente en unas articulaciones que en otras, o puede seguir un patrón atípico de invasión articular.

Las mismas variaciones se observan en la artritis reumatoidea de las articulaciones sacro-iliacas o las apofisarias del raquis.

La artropatía degenerativa (osteoartritis) produce a menudo hallazgos roent-

genológicos bien avanzados antes de manifestarse síntomas. La enfermedad puede ser más o menos generalizada, afectando en particular las articulaciones interfalángicas terminales de los dedos de las manos, la columna vertebral y las grandes articulaciones de los miembros inferiores que sobrellevan el peso. En la espina dorsal los hallazgos radiológicos comprenden alteraciones en los cuerpos de las vértebras (espolones), en los discos intervertebrales (adelgazamiento) y en las articulaciones apofisarias. Todos estos procesos parecen hallarse enlazados. En las articulaciones que cargan el peso, sobre todo la cadera y la rodilla, puede presentarse artropatía degenerativa a consecuencia de esfuerzos continuados impuestos por car-

gas anormales. Las alteraciones radiológicas son semejantes a las observadas en la forma generalizada de la dolencia.

En el hombro, a las periartropatías crónicas corresponden la mayoría de las afecciones incapacitantes, consistiendo la lesión casi siempre en bursitis, tenonitis, o ambas. Aproximadamente en la mitad de estos casos se encontrarán depósitos calcificados en los tendones, mientras que los demás sólo muestran descalcificación crónica de los huesos y contracturas de los tejidos blandos. También se observan depósitos calcificados en enfermos que no tienen síntomas imputables al hombro, de modo que la visualización radiográfica de aquéllos no indica forzosamente la existencia de un proceso inflamatorio crónico.



Röntgen Therapy in Arthritis, Bursitis, and Allied Conditions¹

ERNST A. POHLE, M.D., Ph.D.,² and JAMES A. MORTON, M.D.³

Madison, Wis

THE pathological and radiodiagnostic aspects of arthritis, bursitis, and allied conditions have been discussed in detail in the two preceding papers, by Drs Angevine and Paul (pages 1 and 6). This presentation will relate our experience with the therapeutic use of roentgen rays in these conditions. Roentgen therapy of arthritis is by no means new, since the history of this particular field has been dealt with by several authors (4, 7), suffice it to say that as early as 1898 the subject was mentioned in the French, German, Russian, Swedish and Swiss literature (10). As far as we could ascertain the first American authors dealing with it were Anders, Daland and Pfahler (1), who published a preliminary report of the treatment of arthritis deformans with roentgen rays in 1906. Their results were encouraging and they reached the conclusion that this method is a valuable adjunct in the treatment of these chronic joint affections. In the literature of the last twenty years, however, there are not many references to roentgen therapy of arthritis. This is surprising if one considers the importance of the condition as well as its high incidence. Our report is rendered from a strictly practical standpoint and in an effort to induce more radiologists to try the method in a large number of cases so that we may eventually arrive at its true evaluation.

CLINICAL MATERIAL

During the four-year period 1941-45 we treated 331 separate cases of rheumatoid and hypertrophic arthritis. Early in 1945 we decided to accept as many cases as possible for the present study. All pa-

tients were examined in the diagnostic section of our department and the extent of arthritic involvement was graded. One hundred consecutive cases of arthritis and allied diseases were taken from those treated that year. The results could thus be observed and recorded by the same physician, although it obviated the study of duration of response.

This group of patients is heterogeneous, consisting of state, clinic, and private cases, rural and urban. There was, however, a predominance of farmers, explaining the large number of severe cases of hypertrophic arthritis, a disease which appears to be aggravated by a lifetime of hard work. Ages were well spaced from forty to eighty years, the decade of sixty to seventy having the largest representation. All patients were seen by a member of another department, and many of them were sent to us by the Department of Orthopedic Surgery. All were interviewed by a member of the therapeutic section of our department and the extent of disability was recorded. No objective study was attempted except the taking of roentgenograms in all cases. About 70 per cent of the group were followed by personal interviews, the remainder by mail. Ninety-two cases were traced.

TECHNIC

While in general we do not believe in standardized technic for any one disease, yet most of our cases received essentially the same amount of therapy. We have available a 200-kv (175 constant potential equivalent) and a 400-kv machine, and while osteoarthritis is generally treated

¹ Department of Radiology, University of Wisconsin Medical School, Madison, Wis. Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

² Professor of Radiology, University of Wisconsin.

³ Former Resident in Radiology, University of Wisconsin. Now radiologist, St. Joseph Mercy Hospital, Pontiac, Mich.

TABLE I RESULTS OF ROENTGEN THERAPY IN OSTEOARTHRITIS AND ALLIED CONDITIONS

	Total Areas*	No Relief %	Slight Relief %	Moderate or Complete Relief, %
<hr/>				
Osteoarthritis				
Spine				
Cervical	13	31.0	0	69.0
Thoracic	17	41.0	0	59.0
Lumbar	37	16.0	11.0	73.0
Total	67	25.4	6.0	68.6
Hips	19	31.6	0	68.4
Shoulders	3	33.3	0	66.7
Knees	13	30.8	23.0	46.2
Miscellaneous	3	0	0	100
Total	38	29.0	7.9	63.1
Total all osteoarthritis	105	26.6	6.7	66.7
			<hr/>	
			73.4	
<hr/>				
Rheumatoid Arthritis				
Spine	6	16.7	33.3	50.0
Shoulders	1	100	0	0
Hips	1	100	0	0
Knees	2	0	0	100
Total	10	30.0	20.0	50.0
			<hr/>	
			70.0	
<hr/>				
Bursitis	5	0	20.0	80.0
Periarticular disease	2	50.0	0	50.0
Osteoporosis	4	50.0	0	50.0
Total	11	27.4	9.0	63.6
			<hr/>	
			72.6	

* Total number of different areas in all patients

on the larger machine, the two were used interchangeably as necessity ruled. Physical factors were as follows: for the 200-kv unit, 0.5 mm of copper and 1 mm of Al filter (h v l 1.05 mm Cu), 50 cm target-skin distance, 38 r/minute output, for the 400-kv unit, inherent filtration equivalent to 1.75 mm Cu (h v l 2.4 mm Cu), 50 cm distance, 50 r/minute output. The spinal areas were treated through an 8 × 20 cm port (1 to 3 areas), the smaller joints through 10 × 10 or 15 × 15 cm ports. Spinal areas received 3 × 150 r (in air) on successive days or 3 × 200 r on alternate days. Caution must, of course, be used in treating the lower lumbar region and lumbosacral area in women under forty years of age, since there is a definite possibility of interference with the menstrual cycle. This should be explained to each patient belonging to that group so that she will not become disturbed if it does occur. In younger women we would not recommend the administration of roentgen therapy over these areas for arthritis. For the smaller joints the same

dosage and intervals were used, or smaller doses applied to both anterior and posterior ports. Such therapy will be referred to hereafter as a series of treatments. We do not believe that higher single doses are necessary, although they have been advocated (5). Most patients received one series of treatments, but about 40 per cent had two series, and a small number three. Series were spaced four to six weeks apart. No patient in this study was treated more than three times, although we would give one or two more series after an interval of six months if indicated. With this amount of radiation no permanent harm is done to the skin.

RESULTS IN ARTHRITIS

A comparison of the three total figures underlined in Table I indicates that the response to treatment is in all probability due to a non-specific analgesic effect (2), these totals agree within a few per cent. The number of patients other than those suffering from osteoarthritis is too small for final interpretation, but the agreement

TABLE II AGE DISTRIBUTION AND RESULTS OF ROENTGEN THERAPY IN OSTEOARTHRITIS

Age Group	Per Cent of Total	No Relief %	Slight Relief %	Moderate or Complete Relief %
40-50	16.9	23.1	15.4	61.5
50-60	25.9	10	5	85
60-70	39.0	36.7		63.3
70-80	14.3	36.4	9.1	54.5
80-	3.9	33.3	33.3	33.3

is striking both as to results in similar groups reported elsewhere (8) and in the hypertrophic group in this study. An additional group of 100 cases treated prior to 1945 and selected at random was analyzed and the results were almost identical.

With particular reference to the group of osteoarthritis of the spine (any or all subdivisions of the spine considered one area), approximately 75 per cent of the patients reported moderate to complete relief of pain. All reporting only slight relief had only one series of treatments.

The age of the patient and the severity of the disease are not reliable indications of results to be expected except that there is suggestive evidence that the percentage of good results obtained decreases with advancing age (Tables II and III). Of the 3 patients in the fifth decade of life receiving no benefit, 2 were women with minimal changes in the spine and the other was a male with only moderately advanced disease of one knee. In the fifty to sixty year group 85 per cent had moderate or complete relief of pain, yet 62 per cent of that category had severe changes on x-ray examination. We feel that this latter group represents people still engaged in active life who have both the vitality to "keep moving" and the desire to "get well." What role psychotherapy plays we do not know, since no controls were kept, placebo therapy was not tried. Smyth, Freyberg, and Peck (9) were able to use placebo therapy in cases of rheumatic disease and assign a definite and prominent role to psychotherapy. Our attitude is that if the patient has pain he deserves treatment, if the pain is relieved, the therapy may be considered successful. Nothing more is

TABLE III DEGREE OF INVOLVEMENT AND RESULTS OF ROENTGEN THERAPY IN OSTEOARTHRITIS

Degree of Bony Involvement	No Relief, %	Slight Relief, %	Moderate or Complete Relief, %
Severe	25.5	6.4	68.1
Moderate	10	5	85
Minimum	42.1	10.5	47.4

promised any patient than some relief of pain. The majority of our patients reported disturbance of sleeping habits due to pain, especially after the first and second exposures.

Harmful effects from the treatment are not to be expected, although an occasional one is seen. Sometimes there is an exacerbation of symptoms for a period of one to two weeks and all patients should be warned of this possibility, nausea may occur in those treated over the lumbosacral region. Favorable results, if effected, should not be accepted until three to four weeks following a series. No person should receive any form of local heat or massage to the part under treatment, since this may produce an erythema out of proportion to either the radiation or heat applied. One of our patients had temporary epilation of the hairline from therapy to the cervical spine.

This paper does not cover the question of the duration of relief of symptoms. However, the great majority of the results tabulated were gathered six months after therapy, we believe this period of time to be a fair estimate of the average duration of benefit to be expected in at least 70 per cent of these patients. Two illustrative case reports are given below.

CASE 1 F G, a white male 59 years of age, had had pain in the left hip for the preceding two or three years, particularly marked when driving, when he first went to bed at night, and in the morning. Roentgenograms showed minimal osteoarthritis of the hip joint. In June 1945 the patient received 3×150 r (in air) to the left hip and experienced relief of pain for about one year. At that time there was some recurrence, and a second series was given in August 1946. Partial relief of pain followed, and a third series is planned.

CASE 2 H L, a white female 69 years of age, had had increasing pain in the right hip and low

TABLE IV RESULTS IN ROENTGEN THERAPY IN 69 CASES OF SUBDELTOID BURSITIS

	Complete Relief	Moderate Relief	Slight Relief	No Relief
First series	25 (36.2%)	32 (46.4%)	4 (5.8%)	8 (11.6%)
Second series	6*	1†		
Three or more series	2†			
	84%		16%	

* Only moderate relief after first series

† Only moderate relief after second series

‡ Only slight relief after first series

back for the preceding five or six years. It had become so severe that she was unable to do her housework or to walk outside the house. Roentgenograms showed a transitional vertebra with an articulating transverse process on the right at the lumbosacral junction and severe osteoarthritis of the lumbar spine with moderate changes in the sacroiliac joints and hip joints. Roentgen therapy was administered to the painful right sacroiliac and hip joint areas in January 1945, the dosage was 3×150 r (in air). When the patient returned six weeks later, she reported partial relief of pain and a second series was given. Pain was almost completely relieved and, although some stiffness remains, she has resumed doing her own work and is able to take short walks to see her neighbors.

RESULTS IN BURSITIS

The results of the treatment of bursitis are recorded in Table IV. The response to x-ray therapy was good, either complete or satisfactory relief occurred in 84 per cent of all cases. Although the absolute number of those receiving a second or third series was small, we gained the impression that the additional benefit obtained by further treatment was not striking. Over 50 per cent of all cases showed calcification on roentgen examination before treatment.

In many instances there is a differential diagnostic problem involved, especially in the shoulder region. This has been discussed in detail in the two preceding papers and we will merely state that often it is difficult to differentiate a true bursitis with calcification from what is called peritendinitis calcarea (6). It has been our practice to accept the diagnosis of the orthopedic consultant as based on his clinical and our roentgenographic examinations.

The acute bursitis with agonizing pain, if seen and treated within the first twenty-four hours after the onset, in our opinion stands the best chance for relief, but a

good many of the chronic cases are relieved of pain, and in some a definite increase in the range of motion can be achieved. In these patients, properly supervised exercise should supplement roentgen therapy, for that reason, close co-operation between radiologist and orthopedic surgeon is indispensable.

The technic of treatment is that outlined above. In the acute cases one course of treatment usually suffices and quite frequently reduces the calcification completely or appreciably if this is present at the time treatment is started. Good relief of pain was seen in patients in whom the calcium deposit disappeared as well as in those in whom all of the original deposit remained or was only partially resorbed. Two illustrative case reports are appended.

CASE 1 A white male, age 40, woke up early in the morning of Sept. 25, 1943, with severe pain in the left shoulder. He was unable to move the arm sufficiently to put on his coat. Local application of heat did not bring relief. On the following night the pain became so excruciating that even large doses of morphine did not alleviate it appreciably. Roentgenograms of the shoulder showed a calcium deposit in the region of the subacromial bursa (Fig. 1, A). The clinical findings were typical of bursitis. X-ray therapy was started on Sept. 26, 3×150 r (in air) with a h.v.l. of 1.05 mm in Cu were given to the anterior and posterior left shoulder on three successive days. Within twenty-four hours after the first treatment there was considerable relief of pain. Roentgenograms taken on Oct. 6 showed very little residual calcification and almost normal function of the arm had been restored (Fig. 1, B).

CASE 2 White female, age 66, while visiting in Florida, suffered from a bursitis in the right shoulder. Heat was applied for several days without material relief of pain. On March 29, 1946, a roentgenogram of the right shoulder showed a calcium deposit in the region of the subacromial bursa (Fig. 2, A). The patient was treated there by x-ray— $1/4$ erythema unit—and then returned to Madison. The pain



Fig 1 Bursitis, Case 1 A Roentgenogram taken on Sept 27, 1943 showing calcium deposit (arrow) B Roentgenogram taken on Oct 6 eight days after the last treatment, showing little evidence of residual calcification



Fig 2 Bursitis Case 2 A Roentgenogram taken on March 29 1946, showing calcium deposit (arrow) B Roentgenogram taken on May 20, one month after the last treatment showing little evidence of residual calcification

was temporarily relieved but recurred. She consulted us and received 2×150 r over the anterior and posterior right shoulder with a h v l of 1.05 mm in Cu on April 18 and 19, 1946. Within forty eight hours after the last exposure she was comfortable. Roentgenograms taken on May 20, 1946, showed very little residual calcification (Fig 2, B) and function of the arm was normal.

COMMENT

After a careful analysis of our clinical material, we have reached the conclusion that the prime value of roentgen therapy in chronic arthritis, bursitis, and allied conditions lies in the analgesic effect (3). The same holds true for acute bursitis, although here the action is of a curative na-

ture, since the inflammatory process is itself favorably influenced, as is so well known from our experience in other acute inflammatory conditions. We feel that roentgen therapy has definitely something to offer to this group of patients, whether the effect is entirely due to the analgesic action of the rays or partially due to a psychological factor should not—in our opinion—prevent us from giving the method a fair trial. As to the mechanism of the effect of roentgen rays on osteoarthritis, we have no hypothesis or theory to offer.

In closing, we would like to emphasize that the views presented in this paper are

largely based on our observations in osteoarthritis and bursitis. While we have seen satisfactory response in some patients with rheumatoid arthritis, osteoporosis, and spondylitis rhizomélisque, the number of cases treated is not large enough for statistical analysis.

SUMMARY

1 The experience in the treatment of arthritis and bursitis by roentgen rays in the Department of Radiology, State of Wisconsin General Hospital, has been related.

2 The technic of treatment is described in detail.

3 An analysis of 100 consecutive cases of osteoarthritis reveals that satisfactory relief from pain may be expected in approximately 75 per cent, the corresponding figure for 69 cases of bursitis was 84 per cent.

4 No theory as to the mechanism of the therapeutic effect is offered, we have the impression that it is based on a non-specific analgesic action of the roentgen rays.

Department of Radiology
University of Wisconsin Medical School
Madison 6, Wis

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DISCUSSION OF SYMPOSIUM ON ROENTGEN DIAGNOSIS AND THERAPY OF BURSITIS AND ARTHRITIS

(Papers by D Murray Angevine, Lester W Paul and Wm W Moir, and Ernst A Pohl¹ and James A. Morton)

S Archibald Morton, M D (Milwaukee, Wis) These papers, I feel, offer many interesting points. Dr Paul has covered the subject of diagnosis well. There are many things about calcareous tendinitis that are hard to understand. Why is it—perhaps Dr Paul or Dr Angevine can give us the answer—that we see calcified tendinitis about the shoulder joints so frequently and about the other joints so infrequently? The shoulder is not a weight bearing joint, it is not a joint that is particularly subject to trauma. We do not see calcified tendinitis in the knee joint, for though calcifications are seen about the joint, we do not see them particularly in the tendons.

I believe that it is impossible to examine a shoulder joint adequately with a single film, and I believe all of us should work out some sort of a routine of examination so that all the areas of tendinous insertion will be demonstrated. There may be an area of calcification in a subscapularis tendon which is impossible to demonstrate in anteroposterior films alone. I would like to commend for your use a procedure published by Dr Charles Blackett and Dr Thomas Healy in the *American Journal of Roentgenology* (37 760, 1937).

In my experience I am not able to say very much about the etiological agent on merely looking at a case of arthritis—i.e. whether it is a tuberculous arthritis, septic, gonorrheal, or what not. I believe that the radiologist can say that a destructive arthritis exists, probably tuberculous or probably septic, and that it should be the province of the pathologist to identify specifically the offending agent. All of us have treated these cases of arthritis and bursitis with good results.

I think it is exceedingly difficult to evaluate the effect of treatment in cases with degenerative changes about joints, which we see so frequently. Some patients have pain, some have no pain, and the extent of the involvement does not parallel the amount of pain.

In some of these conditions the trouble is obviously due to mechanical difficulties and it is hard to see just how much roentgen therapy is going to do to the mechanical factors involved. In many of these patients roentgen therapy does not produce very beneficial results. I have had much better results in the treatment of spondylitis rhizomélisque and Marie-Strimpell arthritis than I have in treatment of ordinary degenerative changes about the spine.

The treatment of calcareous tendinitis offers interesting problems too. Do we know whether calcium is the cause of the condition, or its effect?

I would like to ask Dr Pohle if he has had any difference in his results in cases in which calcification was present and those with no calcification. I would like to ask also what his experience has been in those cases that Dr Paul referred to as the "frozen shoulder." In my experience x-ray therapy has done little for such patients, physical therapy has done little for them, and I am not so sure that the great healer "Time" is not better than any of our efforts. In addition to trouble in the shoulder, these patients also have vasomotor tension in the hands, with pain and swelling.

L M Hilt, M D (Eugene, Ore.) During the war we treated quite a few shoulder cases because we did not have time for surgery, and we obtained some remarkable results. They say you know a disease very well if you have it yourself. One day I felt pain in my fingers and right shoulder. I took a film and found I had two small calcifications and one rather large one. As I am left-handed, the question of using the involved shoulder more than the other did not enter into the matter. Within a year's time one series of treatments was sufficient. I have had no symptoms now for about two years. I have treated physicians and others, and, while I have kept no statistics, the results have been most satisfactory.

Vincent W Archer, M D (University, Va.) I am not a therapist but I have heard a great deal this week about the danger of repeated small doses of radiation. In a chronic recurring disease like osteoarthritis, what is going to happen if treatment is followed by relief for six months? Then are you going to repeat the treatment for four months? Wouldn't it be well to use everything else first and resort to irradiation only when other measures fail?

D M Angevine, M D (*closing*) Concerning calcification in the tendons, I do not believe we know the exact mechanism. When one examines a large number of joint capsules from "frozen" joints, however, it is amazing how much calcification there is in such tissues, probably far more than is realized from x-ray examination. I believe that calcification here is probably very much the same as elsewhere in the body. It usually occurs under two conditions: (1) hemorrhage and (2) degeneration of tissue. I believe, therefore, that there must be some degeneration in the joint capsule.

Ernst A Pohle, M D (*closing*) As to the question of Dr Morton, we did not pay any attention to the relationship between calcification present at the time of the treatment and the response, but we did find, as we stated in the paper, that relief from pain was obtained whether or not the calcification disappeared or remained. However, this is an interesting problem and I think from now on we will study it and may be able to give you a report later.

As to the "frozen shoulder," we have had just as little luck as others.

One important point has been raised. Numerous small doses of radiation, if repeated, too often lead, of course, to a late reaction, with the certainty of a planned experiment. As we stated in the paper, we give up to three series from four to six weeks apart. If after six months the symptoms recur, we may give one or two more series and then no more. In our five years of experience, up to now, no late reactions have occurred with this amount of treatment. However, the tolerance varies with the individual and therefore the final decision as to the safe total dose rests with the radiologist.

SUMARIO

Roentgenoterapia de la Artritis, Bursitis, y Estados Afines

Preséntanse las observaciones realizadas en el tratamiento de la artritis y la bursitis con los rayos X en el Departamento de Radiología del Hospital General del Estado de Wisconsin.

El tratamiento fué a base de 200 kv (equivalente potencial constante de 175) (filtración por 0.5 mm de cobre y 1 mm de aluminio, capa de hemi-reducción de 1.05 mm de cobre, 50 cm de distancia foco-piel, 38 r por minuto), o de 400 kv (filtración inherente equivalente a 1.75 mm de cobre, capa de hemi-reducción de 2.4 mm de cobre, 50 cm de distancia, 50 r por minuto). Las zonas raquídeas recibieron 3×150 r (en el aire) en días sucesi-

vos o 3×200 r cada dos días, y las articulaciones más pequeñas una dosis semejante por vía anterior y posterior. En algunos casos repitióse el tratamiento al cabo de cuatro a seis semanas, y en muy pocos se administró una tercera serie.

El análisis de 100 casos consecutivos de osteoartritis revela que cabe esperar alivio satisfactorio del dolor aproximadamente en 75 por ciento, la cifra correspondiente en 69 casos de bursitis fué de 84 por ciento.

No se ofrece ninguna teoría en cuanto al mecanismo del efecto terapéutico, pero existe la impresión de que se basa en una acción analgésica inespecífica de los rayos X.

largely based on our observations in osteoarthritis and bursitis. While we have seen satisfactory response in some patients with rheumatoid arthritis, osteoporosis, and spondylitis rhizomelique, the number of cases treated is not large enough for statistical analysis.

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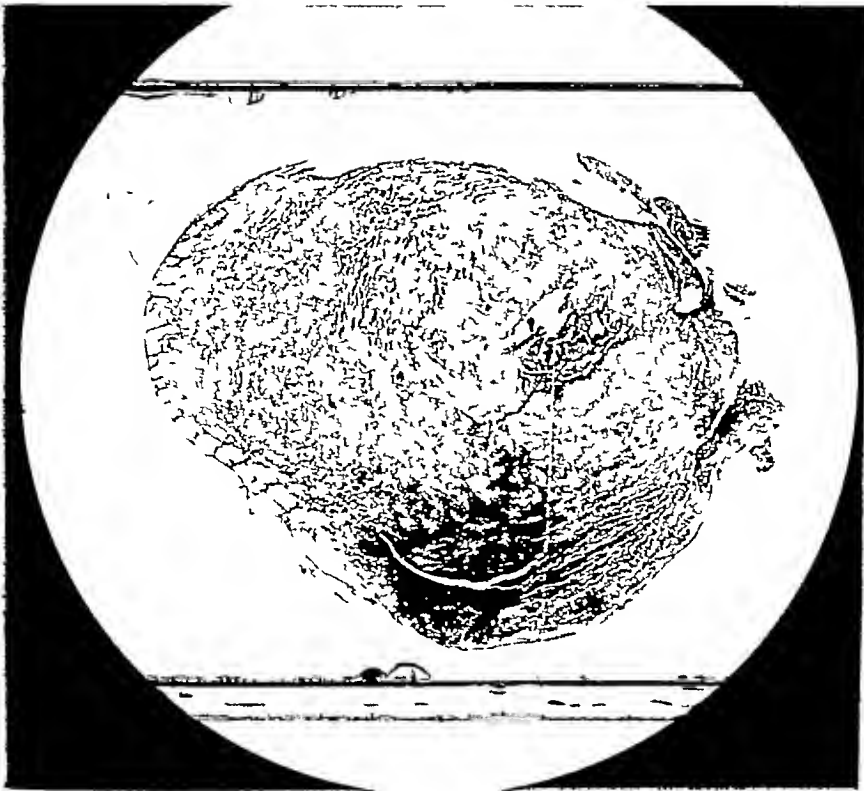


Fig 2 Case 1 Low-power histological sections showing thickening traumatic hemorrhage becoming organized xanthomatous tumor Figures 1 and 2 shown through the courtesy of Doctor Milton Helpert

✓ Roentgen Diagnosis of Pigmented Villonodular Synovitis and Synovial Sarcoma of the Knee Joint

Preliminary Report¹

RAYMOND W LEWIS, M D

Director, Department of Radiology, Hospital for Special Surgery, New York, N Y

IN 1941 Jaffe, Lichtenstein, and Sutro (1) wrote of the pathology of certain diseases of joints, tendon sheaths, and bursae. They showed the histologic linkage and essential unity of lesions previously described in the literature under a wide variety of designations, *i e*, such synovial and bursal lesions as chronic hemorrhagic villous synovitis, giant-cell fibro-hemangioma, fibro-hemosideric sarcoma, sarcoma fusigigantocellulare, benign polymorphocellular tumor of the synovial membrane, and such tenosynovial lesions as xanthoma, xanthogranuloma, giant-cell tumor, and myeloplaxoma. All of these pathological conditions they grouped together under the name of pigmented villonodular synovitis. These same authors wrote that in joints, pigmented villonodular synovitis may occur in circumscribed or diffuse form. In the circumscribed form, the affected synovial membrane shows one or more yellow-brown sessile or stalked tumor-like nodular outgrowths. In the diffuse form (Figs 1 and 2) the membrane appears brownish pigmented and covered by villous and coarse nodular outgrowths. The authors were of the opinion that the condition should not be considered neoplastic, but rather inflammatory in nature, though they had no suggestion to offer with regard to the agent provoking the inflammatory response.

Both pigmented villonodular synovitis and tumors of the knee joint may occur as circumscribed or single lesions (1, 2, 3), and in some instances may be demonstrated roentgenographically (Fig 3). We have thus far been unable from the x-ray appearance alone to do more than hazard a



Fig 1 Case 1 Synovial membrane in pigmented villonodular synovitis showing thickening pigmentation nodular surface, xanthomatous pedunculated tumor

guess as to the character of these solitary lesions. Our principal concern in this communication is with the diffuse synovial lesions, and to these we shall confine our attention.

Although the radiographic characteristics of diffuse villonodular synovitis and diffuse intracapsular tumors of the knee joint, of which synovial sarcoma (synovioma) is the most common, are often identical, the general characteristics of this group are as a rule so typical that, after seeing a few cases, the radiologist is able almost at a glance to classify a new one as belonging in this broad category. These characteristics are as follows (Figs 4-7): bones of a young adult, monoarticular involvement, excessive amount of synovitis, which may appear smooth in outline and homogeneous in density, but is particularly diagnostic when it is, in part at least, nodular in outline and den-

¹ Presented at the Thirty second Annual Meeting of the Radiological Society of North America Chicago Ill Dec 1-6, 1946

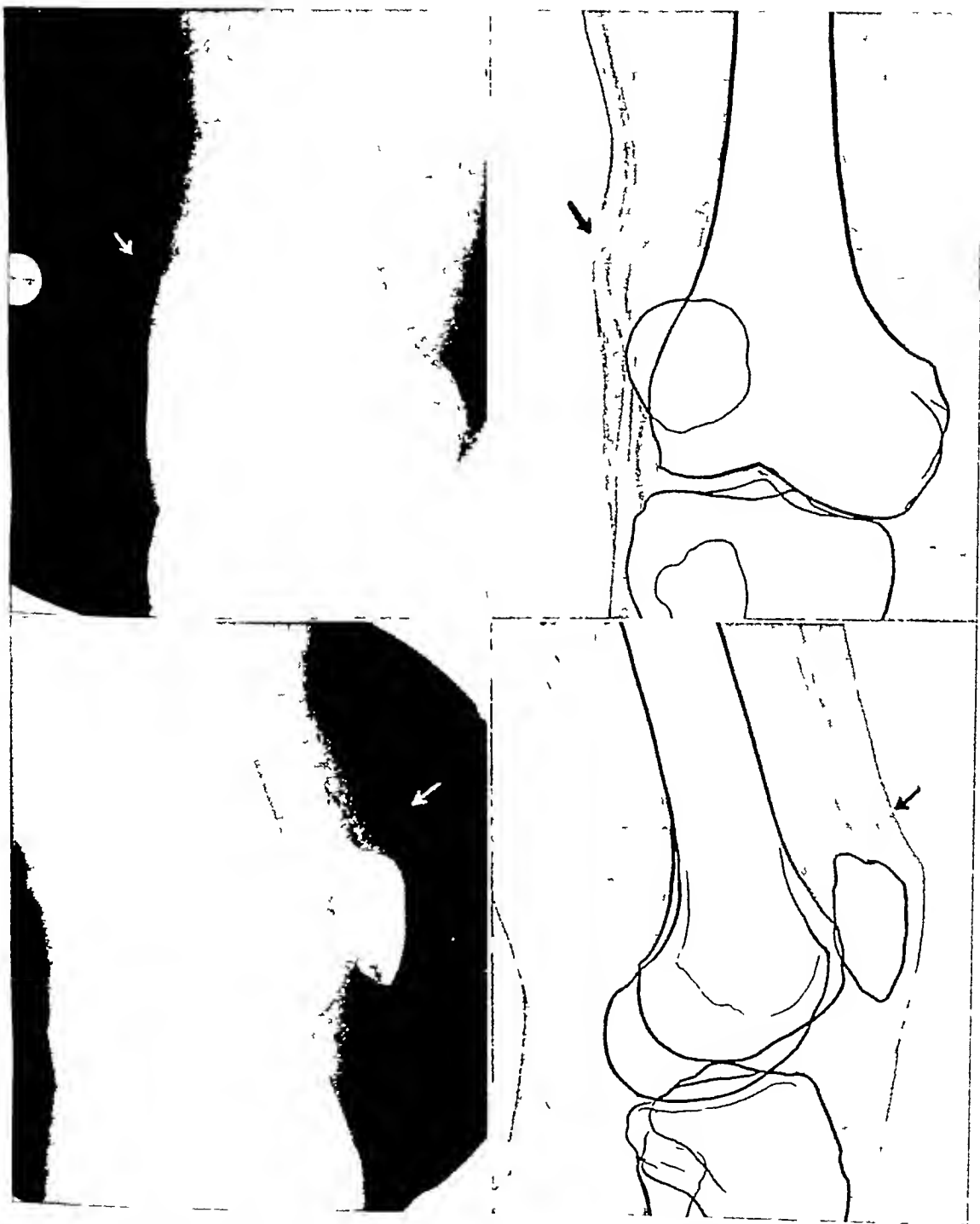


Fig 3 Single tumor hemangioma in knee joint. This might equally well be circumscribed villonodular synovitis. Precise roentgenological diagnosis in single tumors is usually not possible. Reproduced by permission of Am J Roentgenol (5)

sity, as is frequently the case, joint spacing symmetrical and normal, giving no indication of cartilage abnormality, completely normal appearing bones, without even osteoporosis, no evidence of thigh or leg atrophy. in summary, excessive synovitis, often nodular in outline and density, in a young person, with everything else completely normal

Typical history and clinical findings are as follows young adult, rather long history of knee swelling, usually one to several years, no known etiology, though occasionally the onset of the swelling is blamed on some minor injury, relatively little discomfort or disability (the limitation in motion is usually entirely mechanical and due to the synovitis, the rather minor disability explains the absence of osteoporosis), no fever, and normal or somewhat increased sedimentation rate

The differential diagnosis in this group of cases, comprising diffuse villonodular synovitis and diffuse synovial sarcoma, is as follows/ the lobulated and nodular character of the joint swelling is seldom found in other conditions and is therefore a most important differential point. In addition to this, the following are helpful the degree of joint distention is in excess of that usually encountered in traumatic cases without fracture, and the immediate examination excludes the hemorrhage of fracture by excluding fracture. An equal degree of distention occurs in hemophilia, but in that disease there are usually old degenerative changes in cartilage and bone. Against rheumatoid arthritis are the mon-articular character of the lesion, the absence of osteoporosis, which is likely to occur rather early in that disease, and the absence of the symptoms and signs found in rheumatoid arthritis. Against acute infectious arthritis are the presence of more synovitis than one would expect in the early days of that disease, and the absence of acute demineralization of the bone about the joint, which occurs after the first few days. Also the histories of the two conditions are radically different. Against rather early tuberculosis are the absence of

osteoporosis and of thigh or leg atrophy, and the complete absence of pain and disability. Osteoarthritis is excluded by the youthful joint, the absence of degenerative changes in bones and cartilages, and the excessive degree of synovitis

As mentioned earlier, diffuse villonodular synovitis and synovial sarcoma of the knee joint are frequently indistinguishable from each other radiographically (compare Fig 8 with Figs 4, 5, 6, and 7). Nor do the histories and physical examinations aid in the differential diagnosis, for they are practically identical in the two conditions. We have encountered, however, three distinguishing radiographic features, and when any one of the three is present, the disease may be recognized as probably synovial sarcoma and not villonodular synovitis. *First*, if the nodular soft-tissue masses are in part or wholly outside the joint capsule (Fig 9), the lesion is not villonodular synovitis, but may be synovial sarcoma, fibrosarcoma, or some other condition. *Second*, if the lobulated soft-tissue masses in or near the joint contain scattered and irregular deposits of amorphous lime (Fig 10), the lesion is almost certainly a synovial sarcoma (4). *Third*, if the lesion of the soft tissues of the joint has invaded bone (Fig 11), the condition is probably synovial sarcoma.

This report has been labeled preliminary because of the few proved cases. There are 4 cases proved by operation, with 7 additional cases which are characteristic clinically and roentgenographically but which have not been operated upon. The lack of success attending synovectomy in our early cases was so striking that the later cases were for the most part not subjected to surgery. Hence our low incidence of proved cases. In view, however, of the importance of establishing a precise diagnosis, and especially of differentiating the synovioma cases from those of villonodular synovitis, exploratory operation and biopsy would seem definitely indicated, and it is possible that this may become the accepted practice of the future.

Although therapy is not rightly included

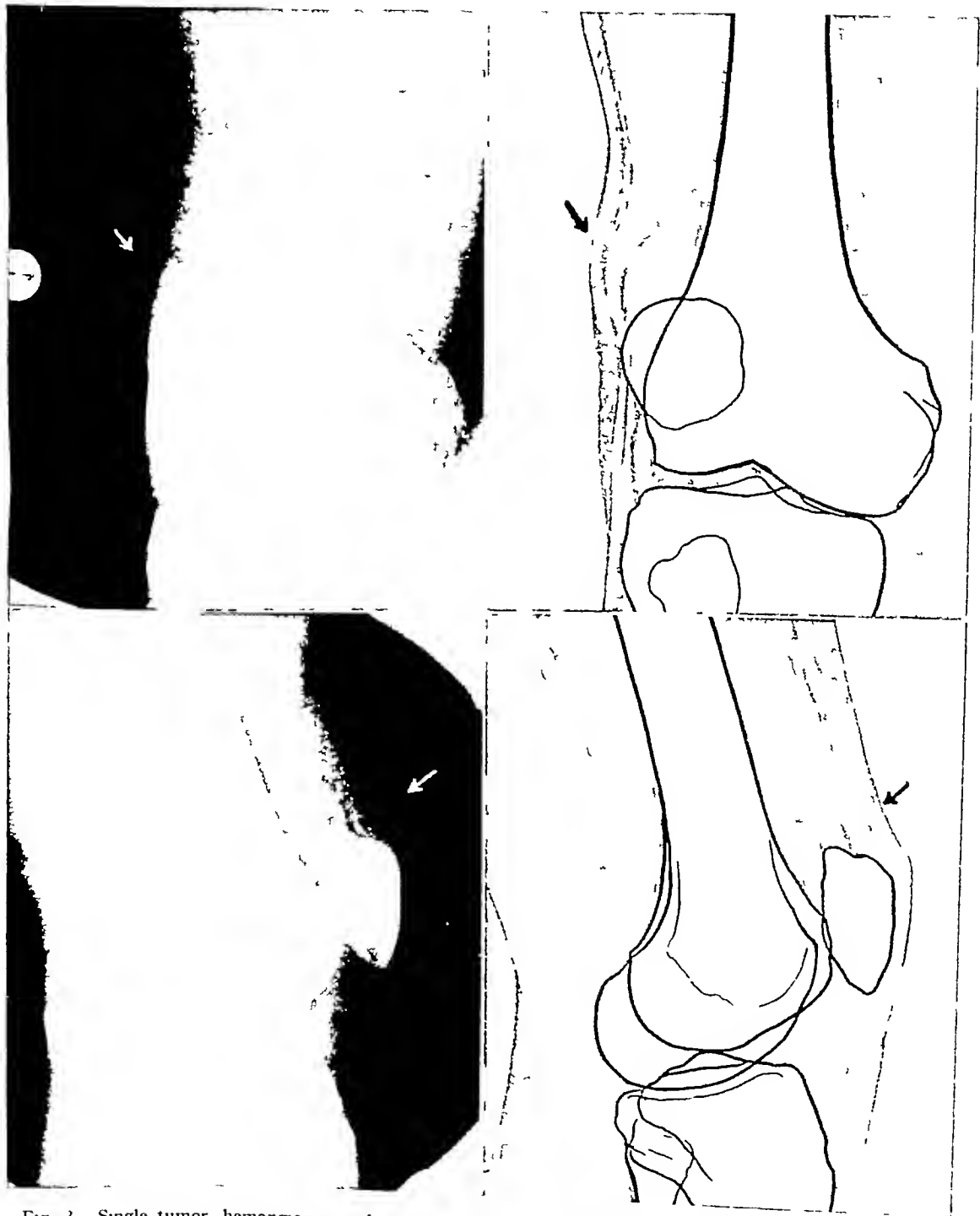


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 of Am J Roentgenol (5) Reproduced by permission

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Although therapy is not rightly included



Case 2 Pigmented villonodular synovitis Findings similar to those in Case 1 shown in Figure 4 The nodular pattern is especially evident in the posterior portion of the joint



Fig 4 Case 1 Pigmented villonodular synovitis of characteristic appearance extreme synovitis with nodular pattern joint spacing normal and symmetrical giving no indication of cartilage abnormality completely normal appearing bones without even osteoporosis



Fig 7 Case 4 Pigmented villonodular synovitis Extreme generalized synovitis but in this instance the pattern is not definitely nodular There is no suggestion of bone or cartilage abnormality



Fig 8 Synovioma, synovial sarcoma in this instance not distinguishable radiographically from the pigmented villonodular synovitis cases shown in Figures 4-7
Reproduced by permission of Dr D A De Santo and Surg, Gynec and Obst. (3)

knee joint showed no growth, and guinea-pig inoculation gave no evidence of tuberculosis

The findings on x-ray examination are shown in Figure 4

Conservative treatment in plaster brought no improvement, and synovectomy was done on Feb 5, 1943. The pathologist's report was chronic proliferative and hemorrhagic villous synovitis with hemosiderosis and xanthomatous formation

Synovectomy was again done on May 19, 1944. The report of the pathologist was chronic proliferative pigmented villonodular synovitis

Examination on Oct 15 1945 showed clinical and

roentgenographic evidence of recurrence. There was some pain in the knee. Range of motion was limited to 30 degrees of flexion from full extension. The patient left this hospital, but it has been learned that she is receiving x-ray therapy elsewhere

CASE 2 F C, female, age 29, came to the clinic April 2, 1943, with swelling of the left knee of two years duration. There had been no injury or other known etiology. Examination showed a distended joint, with a soft tissue mass in the popliteal space. There was fairly good range of motion, with flexion restricted beyond 130 degrees. The blood count was normal. Sedimentation rate 51 mm in one hour. A



Fig 6 Case 3 Pigmented villonodular synovitis Findings similar to those in Case 2 Figure 5 with the nodular pattern particularly noticeable posteriorly Shown through the courtesy of Lt Col E C Holscher Chief of Orthopedic Section Lawson General Hospital

in this presentation, a few brief remarks on treatment seem in order. Surgery seems to have failed completely in relieving villonodular synovitis. Our first patient had a recurrence after two attempts at complete synovectomy. In our second patient, a second operation was necessary to remove large calcareous and osseous bodies which formed in the suprapatellar pouch following the first operation. This patient was then lost track of before we learned the final outcome. In the third proved case, shown through the courtesy of Lt Col E C Holscher, Chief of the Orthopedic Section, Lawson General Hospital, there had been no evidence of recurrence during a short follow-up period. The outcome, however, seems dubious, since the pre-operative roentgenograms showed much involvement of the posterior portion of the joint, and it is known that this region was not cleaned out adequately at operation. In another case of Colonel Holscher, not included in this series because the pre-operative films were not available, there

was recurrence following surgery. In our fourth and very recent case, the result is not yet known. That is, in 5 cases treated by operation, results are known to be unsatisfactory in 3, the outlook is dubious in the fourth, and the result is as yet unknown in the fifth.

Jaffe and Lichtenstein (6) report good results in villonodular synovitis following roentgen-ray therapy, and Friedman and Ginzler (7) describe radiation treatment of one case with an excellent outcome. We at our hospital are trying this medium, but have as yet no results to report.

CASE REPORTS

CASE 1 E Van V female, age 20 came to the clinic Nov 24, 1942, with swelling of the left knee, present for a year and a half. The onset occurred after bumping the knee on a chair under the table. The patient had been seen by several doctors without improvement.

Examination showed much swelling of the knee but free motion, lacking only 30 degrees of complete flexion. The blood count was normal. Sedimentation rate 11 mm in one hour. The Kline reaction was negative. Culture of fluid aspirated from the



Fig 7 Case 4 Pigmented villonodular synovitis Extreme generalized synovitis but in this instance the pattern is not definitely nodular There is no suggestion of bone or cartilage abnormality

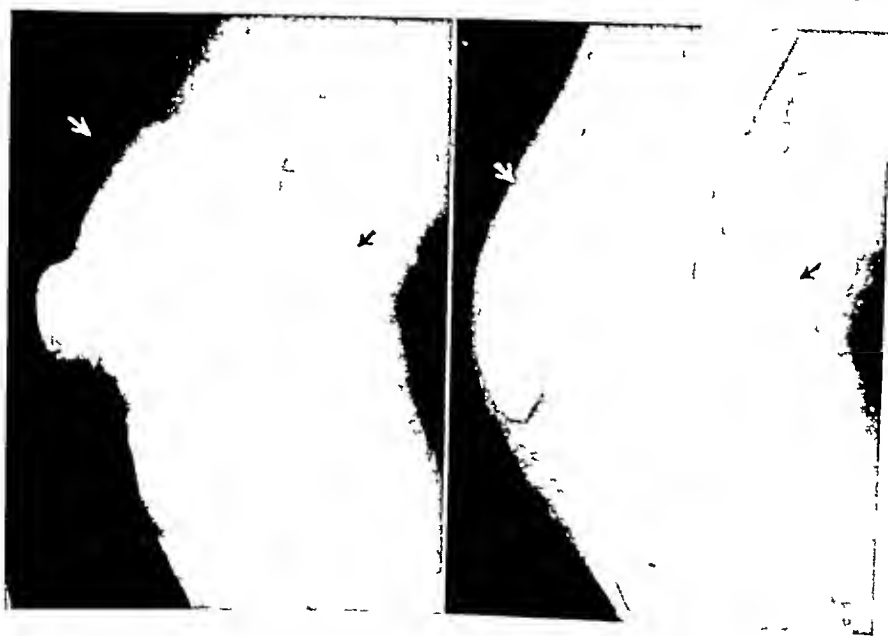


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Reproduced by permission of Dr D A De Santo and Surg, Gynec and Obst (3)

knee joint showed no growth, and guinea-pig inoculation gave no evidence of tuberculosis

The findings on x ray examination are shown in Figure 4

Conservative treatment in plaster brought no improvement and synovectomy was done on Feb 10, 1943. The pathologist's report was chronic proliferative and hemorrhagic villous synovitis with hemosiderosis and xanthomatous formation

Synovectomy was again done on May 19, 1944. The report of the pathologist was chronic proliferative pigmented villonodular synovitis

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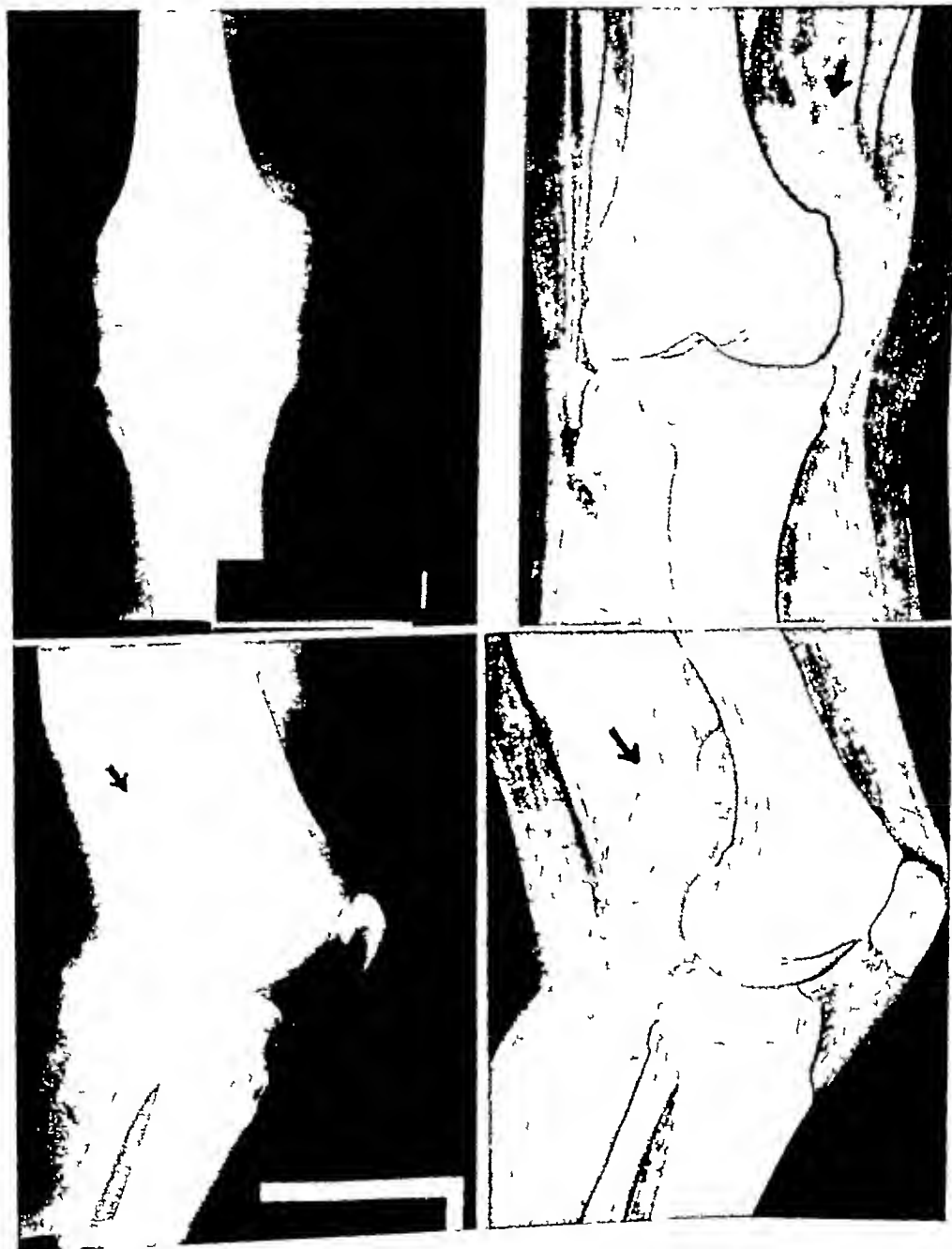


Fig 9 Synovioma synovial sarcoma. This case can be differentiated radiographically from pigmented villonodular synovitis because there is no generalized synovitis since the suprapatellar and infrapatellar portions of the joint are found entirely clear. Therefore the nodular soft tissue mass in the popliteal space is probably extracapsular and the roentgen diagnosis is tumor of some sort.

Smear of fluid aspirated from the knee joint revealed no organisms. Culture of the fluid yielded no growth, and guinea-pig inoculation produced no evidence of tuberculosis.

X-ray examination was as shown in Figure 5.

Conservative treatment in plaster brought no improvement, and on July 2, 1943, synovectomy was performed. The pathological report was chronic pigmented proliferative villonodular synovitis.

A second operation was performed Nov. 12, 1943,



Fig 10 Synovioma synovial sarcoma This case can be differentiated from pigmented villonodular synovitis because of the scattered and irregular deposits of amorphous lime in the lobulated soft-tissue masses Radiographically this can be identified with a reasonable degree of certainty as synovial sarcoma Reproduced by permission of Am J Roentgenol (4)

for removal of calcifications and ossifications from the quadriceps pouch The report of the pathologist was proliferated osseous bodies following synovectomy for villonodular synovitis

The patient was last seen at the hospital Jan 26, 1944, two and a half months after the second operation, at which time there was no evidence of recurrence, and motion was from full extension to 45 degrees flexion She did not return again, or respond to requests that she attend the follow-up clinic

CASE 3 (reported through the courtesy of Lt Col E C Holscher) F L P male technical sergeant, age 38, gave a history of chronic recurrent synovitis for several years monarticular right knee There was no history of injury

X-ray examination was as shown in Figure 6

At operation the condition appeared like an old chronic hemorrhagic synovitis No gross xanthomatous lesions were found The report from the Army Institute of Pathology was pigmented villous synovitis

During the short period the patient was followed after operation there was no evidence of recurrence,

but it is known that the abnormal tissue at the back of the joint was not completely removed

CASE 4 A W, female, age 44, came to the clinic March 28, 1946, complaining of pain and swelling of the right knee, of one year's duration There was no known cause Examination showed no limp There was swelling, but no tenderness and no pain on manipulation A normal range of motion was present

X-ray examination, April 1, 1946, showed a rounded density in the suprapatellar pouch of the joint, concerning which the suggestion was made that it might be exudate or a tumor mass There was evidence of some generalized synovitis, there was no indication of cartilage abnormality

On April 25, 1946, the sedimentation rate was 37 mm in one hour

X-ray examination Sept 4, 1946 (Figure 7) gave findings much like those in the examination five months before The appearance was believed consistent with pigmented villonodular synovitis

At operation—Sept 6, 1946—the synovium was found to be very thick and much inflamed Villous nodules were present in the intercondylar space



Fig 11 Synovioma synovial sarcoma recognizable as not pigmented villonodular synovitis because the soft-tissue lesion of the joint has invaded bone The probable x ray diagnosis is therefore synovial sarcoma

Radical synovectomy was performed. The report of the pathologist was pigmented villonodular synovitis.

The postoperative course was uncomplicated. Radiation therapy was started, and the patient was discharged Oct 1, 1946.

SUMMARY

1 The pathology of pigmented villonodular synovitis as described by Jaffe, Lichtenstein, and Sutro has been briefly reviewed, and illustrations have been shown.

2 Circumscribed pigmented villonodular synovitis and single tumors of the knee joint are often demonstrable by x-ray, but can seldom be diagnosed precisely.

3 The distinctive characteristics of diffuse pigmented villonodular synovitis and synovial sarcoma of the knee joint, which are frequently indistinguishable from each other, have been described and illustrated.

4 Typical histories and physical findings of this group, and features for its differential diagnosis from other conditions, have been given.

5 Three distinguishing radiographic features by which synovial sarcoma may sometimes be differentiated from diffuse villonodular synovitis have been mentioned and illustrated.

6 We have few proved cases of villonodular synovitis because surgical treatment proved completely unsatisfactory in our early cases, and the later clinically and radiographically diagnosed cases were not subjected to surgery. In view of the importance of establishing precise diagnoses, and especially of differentiating synovial sarcoma from villonodular synovitis, exploratory operation and biopsy seem indicated.

There is some evidence that roentgen-ray therapy influences pigmented villonodular synovitis favorably.

NOTE: The author wishes to express his gratitude to Mrs. Olive Fischer for the excellent drawings and illustrations in this article and in previous publications.

321 East 42nd St.
New York 17 N. Y.

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DISCUSSION

Jacob Gershon-Cohen, M.D. (Philadelphia, Penna.) We have been privileged to listen to an excellent presentation, one which is of very material help in an analysis and appreciation of soft-tissue masses and tumors around the joints, particularly the knee joint. This contribution by Dr. Lewis on pigmented villonodular synovitis is significant because (1) it has given serious recognition to the important pathological investigations by Jaffe and his group, (2) it has shown a skillful roentgenological approach to these newer pathologic concepts, (3) it has demonstrated again the importance of roentgenographic soft tissue shadows, and (4), it has shown Dr. Lewis to be a keen clinical observer since this report drives an important wedge into the problem of understanding more precisely soft-tissue diseases of the joints, particularly of the knee.

The use of the word 'synovioma' to designate a particular type of tumor of the synovial membrane, or to imply a sarcoma or even a broader group of other synovial membrane tumors, probably has no place in such a precise report as this, but the very use of this word demonstrates that we still have a stretch of blind road ahead of us before we come to the labeled avenues of synovial physiology and pathology.

The occurrence of pigmented villonodular synovitis in the young raises a suspicion of a mechanism at play similar to that which results in osteochondritis, and there is no reason why some radiologist rather than a sequestered laboratory worker should not some day discover that a transient hypovitaminosis or an avitaminosis during adolescence leads to this roentgenologic entity.

There is also room for more observation of this condition during adult and late life. Does the synovial change of this entity during adolescence lead to chondromatous synovitis or osteochondromatosis during adult life? This may not be a far-

fetched possibility when one remembers that the synovial membrane contains cells capable of metaplasia into cartilage or osteoblastic cells

The suggestion made by Dr Lewis of the good

effects obtained with roentgen therapy should be vigorously pursued, especially since synovectomy has not proved too promising in the treatment of this condition

SUMARIO

Diagnóstico Roentgenológico de la Sinovitis Pilonodular Pigmentada y del Sarcoma Sinovial de la Articulación de la Rodilla Informe Preliminar

La sinovitis pilonodular pigmentada comprende varios estados patológicos descritos con distintos nombres, pudiendo presentarse en forma circunscrita o difusa en las articulaciones. Sobre la última forma es que versa este trabajo.

El cuadro radiográfico de la sinovitis pilonodular pigmentada difusa y del sarcoma sinovial de la articulación de la rodilla, que son frecuentemente indistinguibles, es típico, consistiendo en hipersinovitis, a menudo de contorno y densidad nodulares, en una persona joven, en la cual todos los demás datos son completamente normales. Las principales características clínicas comprenden edema de la rodilla, relativamente leves malestar e incapacidad, apirexia y eritrosedimentación normal o poco aumentada.

Al señalar las características que diferencian este grupo clínico de otros estados, mencionanse e ilustranse tres rasgos radiográficos que permiten a veces distinguir el sarcoma sinovial, de la sinovitis pilonodular difusa, y son los siguientes. Primero, si los tejidos blandos nodulares quedan

total o parcialmente fuera de la cápsula articular, no se trata de sinovitis pilonodular, pudiendo la lesión ser sarcoma, fibrosarcoma o algún otro estado sinovial. Segundo, si las masas de tejido blando lobulado en la articulación o cerca de ésta contienen depósitos irregulares y esparcidos de cal amorfa, trátase casi seguramente de sarcoma sinovial. Tercero, si la lesión del tejido blando de la articulación se ha extendido al hueso, el estado es probablemente sarcoma sinovial.

El autor cuenta con pocos casos comprobados de sinovitis pilonodular, porque el tratamiento quirúrgico resultó ser un completo fracaso en los primeros casos, y no fué utilizado en los últimos casos diagnosticados clínicamente y radiográficamente. Vista la importancia de establecer el diagnóstico preciso, y en particular de diferenciar el sarcoma sinovial de la sinovitis pilonodular, parecen hallarse indicadas la exploración operatoria y la biopsia.

Hay algunos indicios de que la roentgenoterapia afecta favorablemente la sinovitis pilonodular pigmentada.



Appendiceal Coproliths Their Surgical Importance¹

SYDNEY F THOMAS, M D

Palo Alto, Calif.

THE CLINICAL diagnosis of appendicitis is still a major medical problem, not only because of its frequency but because of the morbidity which is associated with the condition, not to mention a mortality of over 17,000 deaths per year in the United States. The literature has been saturated with data on the cause, diagnosis, and treatment of the disease, in 1931 McClure (1) reported that over 9,000 articles had been written on appendicitis, and to that number over 3,000 have since been added, making a total of 12,000 articles. Even though great strides have been made in the technic of appendectomy, and despite the use of the more recent antibiotics (sulfa drugs and penicillin), the morbidity is still considerable and complications remain a serious hazard. In one large clinic (2) the complication rate is unchanged over a period of 19 years. The common origin of the complications in some mechanical factor must therefore be considered.

Roux (3) in 1913 was the first to write on the use of roentgen rays in the diagnosis of appendicitis. The early radiologic diagnosis of uncomplicated appendicitis is difficult and seldom essayed. However, when perforation has occurred with peri-appendiceal abscess formation, free peritoneal gas, peritonitis, subphrenic or subhepatic abscess, or even fistula formation, roentgen studies can give *prima facie* evidence not only localizing the disease but often exhibiting its extent. The early clinical diagnosis is recognized as all-important in appendicitis, but often the

clinical signs are few and the history unconvincing, or possibly all signs and symptoms may be subsiding when the patient is first seen. It is in this group of cases—or at least a percentage of them—that the radiologist might be useful, especially where the appendix is found to contain a coprolith with enough calcium to cast a shadow on the roentgenogram.²

Because of the morbidity in 4 of the cases in our small series, it was thought wise to emphasize the importance of a roentgenographic diagnosis of appendiceal coprolith. The significance of this diagnosis is obvious when one reviews the literature on appendicitis and finds that the most frequently mentioned cause is appendiceal obstruction.

There are two types of appendiceal obstruction: (a) that due to external causes—a kink and/or adhesions, (b) that due to internal causes, namely, foreign bodies, including fecaliths (4). It is in the latter group that we are especially interested because the more severe complications occur following rupture of the appendix due to obstruction by a fecalith, that is, an internal obstruction. The actual blocking of the lumen is considered only the precursor of the obstruction of the lymphatic and blood supply which produces gangrene of the appendiceal wall (4, 5).

The demonstration of appendiceal coproliths which contain enough calcium to be visible radiographically is important not *per se*, but for the implications inherent in their presence. Since the *nidus* or inspissated fecal collection (which forms

¹ Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill. Dec. 1-6, 1946.

The cases reported were seen at the U. S. Naval Hospital, Oakland, Calif., and in the Department of Radiology, Stanford University Medical School, San Francisco, Calif., and the Palo Alto Clinic. The opinions and comments are those of the author and do not in any way represent official opinions or reflect the views of the Navy Department.

² The word coprolith (dung stone) is used in this article to emphasize the radiopacity of the fecalith or enterolith described. In the older literature the words fecalith and concretion are used liberally to mean an inspissated fecal collection in the appendix. Many of these contain only small amounts of calcium but a few can be dignified by the term calculus or coprolith.

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clinical signs are few and the history unconvincing, or possibly all signs and symptoms may be subsiding when the patient is first seen. It is in this group of cases—or at least a percentage of them—that the radiologist might be useful, especially where the appendix is found to contain a coprolith with enough calcium to cast a shadow on the roentgenogram.²

Because of the morbidity in 4 of the cases in our small series, it was thought wise to emphasize the importance of a roentgenographic diagnosis of appendiceal coprolith. The significance of this diagnosis is obvious when one reviews the literature on appendicitis and finds that the most frequently mentioned cause is appendiceal obstruction.

There are two types of appendiceal obstruction: (a) that due to external causes—a kink and/or adhesions, (b) that due to internal causes, namely, foreign bodies, including fecaliths (4). It is in the latter group that we are especially interested because the more severe complications occur following rupture of the appendix due to obstruction by a fecalith, that is, an internal obstruction. The actual blocking of the lumen is considered only the precursor of the obstruction of the lymphatic and blood supply which produces gangrene of the appendiceal wall (4, 5).

The demonstration of appendiceal coproliths which contain enough calcium to be visible radiographically is important not *per se*, but for the implications inherent in their presence. Since the nidus or inspissated fecal collection (which forms

¹ Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

The cases reported were seen at the U. S. Naval Hospital, Oakland, Calif., and in the Department of Radiology, Stanford University Medical School, San Francisco, Calif., and the Palo Alto Clinic. The opinions and comments are those of the author and do not in any way represent official opinions or reflect the views of the Navy Department.

² The word coprolith (dung stone) is used in this article to emphasize the radiopacity of the fecalith or enterolith described. In the older literature the words fecalith and concretion are used liberally to mean an inspissated fecal collection in the appendix. Many of these contain only small amounts of calcium but a few can be dignified by the term calculus or coprolith.



Fig 1 Case I A The spherical, dense laminated 7-mm coprolith is seen overlying the right side of the posterior pelvic space (lamination not clearly visible in reproduction)
 B Because the patient had 1-2 red blood cells in his urine an excretory urogram was done and the ureter can be seen just lateral to the coprolith

the center of a coprolith) with inspissated mucus and cellular debris has remained in the appendix long enough to become calcified, the possibility (and probability) of internal obstruction is present and, like a gallbladder which contains stones, the wall of the appendix shows chronic inflammation (6), which may make it more likely to be perforated (7) Vaughan (8) agrees with this and states that the important point to bear in mind is that the concretum and perforation bear a cause-and-effect relationship

In the literature, one finds enough isolated instances (6, 9, 10, 11) of recurrent pain and recurrent appendicitis caused by appendiceal coproliths to warrant further emphasis on the calcifications in the right lower abdomen which too often go unclassified or unmentioned Shelley, for example, reported a case (12), which has been abstracted in the *Year Book of Radiology* The succinct words of the abstract bring out the points well "He states that,

had a diagnosis of the condition been made from a roentgenogram made more than four months before the onset of the attack of acute suppurative (perforating) appendicitis, the patient would have been spared the ordeal through which he went and which almost cost him his life" (See also Case IV, below) Steinert *et al* (13) write "When appendiceal concretion is demonstrated by roentgenologic examination as a secondary finding, there is possibly reason for suggesting prophylactic appendectomy, even if at the moment the patient has no symptoms from appendicitis" Tripodi and Kruger (14) express themselves in even stronger terms, on the subject of appendiceal lithiasis "When definitely diagnosed, surgery is indicated, as a superimposed acute inflammatory process with perforation may occur as a major complication"

Coproliths may be single or multiple and must be differentiated from gallstones, urinary calculi, mesenteric calcifications

phleboliths, retained radiographic medium, and even calcified appendices epiploicae (33). If the suspicious shadow has a laminated structure (Figs 3 and 4) which is extrinsic to the urinary tract and out of the pelvis (away from the usual location of phleboliths), the possibility of an appendiceal coprolith must be kept in mind. With such evidence, the decision to operate could be made even in the face of subsiding symptoms or an atypical history. If the roentgenogram reveals an opacity in the right lower quadrant overlying the usual course of the urinary tract, operation may be delayed pending the results of a urogram (15, 16, 17), especially if the findings in the urine are questionable (Case I, Fig 1). The differential diagnosis is not complete without the exclusion of gallstones (16), as the gallbladder may occasionally be abnormally low or the cecum with the appendix may lie unusually high (Figs 2 and 4). Phleboliths can usually be differentiated from an appendiceal concretion by the character of the calcification. The phlebolith is usually uniformly calcified and rarely contains concentric layers. The phlebolith is practically always spherical while the coprolith is not necessarily so. The immobility and the pelvic location of the phleboliths are further differential points.

Most calcifications in the abdomen, if at all irregular and not overlying the biliary or urinary tract, are accepted as calcifications in mesenteric nodes, but care should be taken not to overlook an appendiceal coprolith. The irregular character of the calcification in a mesenteric node, coupled with its mobility, makes confusion with an appendiceal coprolith unlikely if one is cognizant of the need for differentiation.

How often are appendiceal fecaliths opaque enough to cast a roentgen shadow? Stemert *et al* (13), in a recent study of 104 roentgenograms of patients with acute appendicitis, found that in 10 per cent of the cases there were fecaliths containing enough calcium to be demonstrable roent-



Fig 1 C A roentgenogram of the partially barium filled cecum shows a defect on its posterior inferior portion, and lying in the center of the defect the coprolith (between the arrows), partially obscured by the barium. The irregular collection of barium at the base of the lowest of the small arrows probably lies in the abscess pocket found at surgery.

genographically. The general incidence of fecaliths (calcified or uncalcified) has been estimated by various authors (Graham and Guthrie, 18, Bunch and Adcock, 19, Aschoff 20) at 60 per cent. In one series (13) 30 per cent of the appendiceal fecaliths were sufficiently opaque to show on roentgenograms of the abdomen. Roentgenographic studies of fecaliths found on routine pathological study of surgical and autopsy material at Stanford and San Francisco Hospitals have clearly demonstrated that the vast majority contain calcium, but only 25 per cent appear to be opaque enough to be seen on an abdominal film.

Archibald found 22 concretions in the appendix in 41 cases of perforation, but only 3 in 38 non-perforating cases. Bowen discovered concretions in 80 per cent of "abscessing" or gangrenous appendices and in only 9 per cent of catarrhal appendices (7).



Fig 2 Case II The large 14 mm laminated coprolith and multiple (15) smaller coproliths are shown as they were discovered at the time of the gall bladder study. A urogram demonstrated that the opacities were outside the urinary tract. A barium enema study showed their constant proximity to the cecum. The appendix could not be filled. The roentgenogram of the appendix after removal with the multiple coproliths demonstrates their character and their relationship to one another.

CASE HISTORIES

CASE I On Feb 4, 1945, J F G, a 17-year old white boy was seized suddenly with steady mid-abdominal pain, not cramp like in nature. He complained of nausea and vomited about ten hours later. On admission to the hospital, Feb 6 he was obviously ill, restless, and trying to find a position to relieve the pain. His pulse was 92, temperature

100.6°. The abdomen was moderately rigid, with more resistance on the right. There was moderate rebound tenderness referred to the left side of the abdomen, and peristalsis was present. A rectal examination was negative. Examination of the head and chest revealed no disease. The white blood cell count was 23,000 (82 per cent polymorphonuclears, 25 per cent banded forms). The urine showed 1-2 rbc/hdf.

Impression Acute inflammatory process in the abdomen, probably appendicitis.

The patient was treated conservatively because the diagnosis was uncertain, the course was at a standstill, and penicillin was available.

Pain and tenderness gradually subsided. After three weeks' observation, x-ray examinations were completed (Fig 1). On March 6 an appendectomy was done. Adhesions were found in the right lower quadrant and severed. The cecum was mobilized, and the base of the appendix found. The detached tip of the completely divided appendix was seen. A small abscess containing a coprolith was connected with the cecum through a fistula. The stump and tip of the appendix were removed, and the hole in the cecum repaired. The abscess was drained after removal of the coprolith. The patient was returned to duty on April 19, after a thirty-day leave, three and a half months after entry.

The coprolith was very hard and could not be crushed with a curved clamp. Histologically the wall of the appendix was found to be thickened, with hypertrophy of the musculature, and infiltrated with round cells.

CASE II On March 12, 1945, O C A, 33 years old, entered the hospital, reporting that on Feb 27 his shipmates had told him that his skin was yellow (jaundiced). He had had a severe headache with other minor prodromal symptoms for two to three days prior to this.

Physical examination revealed yellow sclera and skin. The liver was palpable and slightly tender. Liver function tests and the clinical course pointed to a mild attack of hepatitis, recovery from which was rapid. To complete the work up, a cholecystogram was obtained on May 16, and the roentgenologist reported a normally functioning gallbladder and multiple calculi in the appendix (Fig 2). This was followed by excretory urography and a barium enema study to verify the location of the coproliths.

When a more detailed history was taken, emphasizing the colicky type of pain, it was discovered that there had been recurrent attacks of right lower quadrant pain of a minor nature for two or three years. An appendectomy was done on June 19, 1945. The postoperative course was uneventful and the patient was sent back to duty on July 19.

The muscular wall of the appendix was remarkably thickened especially over the largest coprolith. The lymphocytic infiltration of the wall was only moderate.

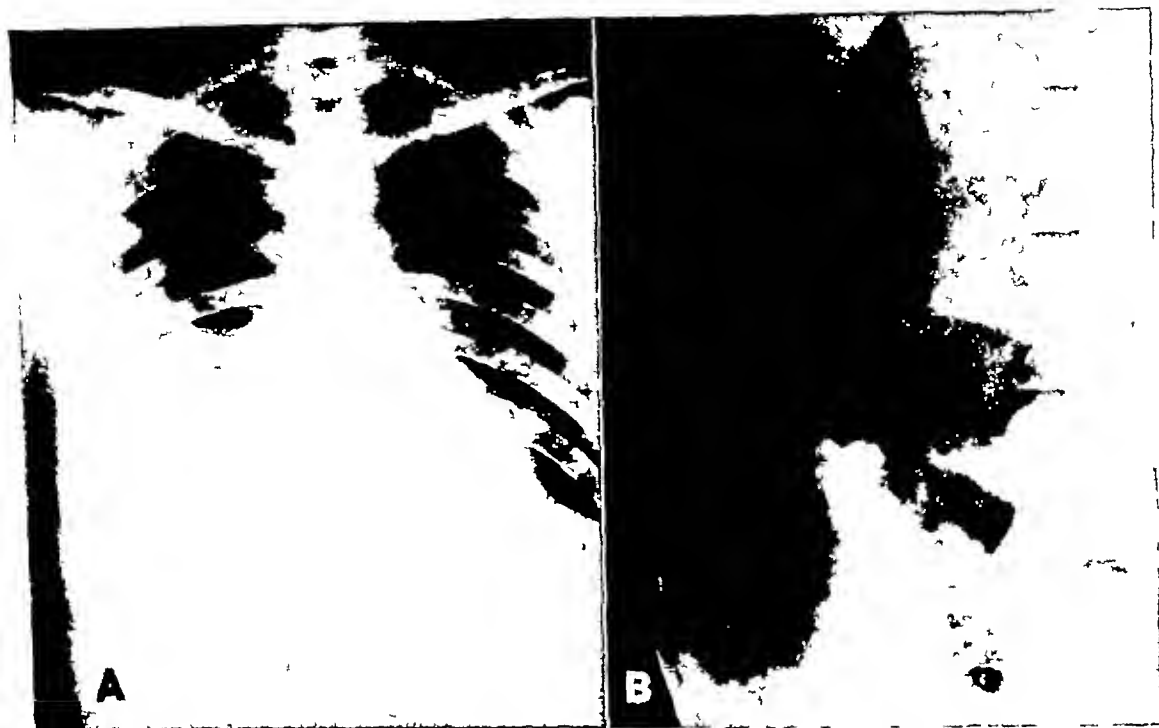


Fig 3 Case III A Roentgenogram of the chest made overseas at the time the patient had a pleural effusion secondary to the subphrenic abscess. Note the elevated right leaf of the diaphragm.
 B The large 20 mm laminated coprolith with the smaller 7-mm coprolith lying more superiorly. An excretory urogram demonstrated the course of the ureter medial to the opacities.

CASE III W B, 24 years old, was admitted May 14, 1945, from an overseas hospital. His health record of March 27, when he was first hospitalized, pictured a very ill young man with an erysipeloid lesion over the abdomen, a high fever, and leukocytosis. A pleural effusion developed (Fig 3, A) and finally, after three weeks, an obvious subphrenic abscess was diagnosed and drained (April 19). It was described as being posterior to the liver. Cultures were made and *E coli* and *B proteus* were reported.

Upon the patient's arrival at this hospital, the abdominal wound was still draining and occasionally there was a low grade fever. After the initial white blood count of 12,000 dropped to 9,600, with differential counts showing a slight shift toward the left, examination directed to the cause of the subphrenic abscess was started. A roentgenogram of the chest revealed almost complete clearing of the pleural effusion and only slight elevation of the right leaf of the diaphragm. In a roentgenogram of the abdomen 2 opacities were seen in the right lower quadrant (Fig 3 B) and appendiceal coproliths were suggested by the roentgenologist. Further studies, including an excretory urogram and barium enema examination (Fig 3 C) were done. It was only after the suggestion of appendiceal coproliths was made that the ward medical officer elicited a history of abdominal pain in 1942 when the patient had

intermittent cramp like pains, severe enough to cause him to "double up." The most severe attack lasted two weeks, when he was in bed with almost persistent abdominal pain. He had no further complaints until his present illness, when, on March 30, 1945, five days after the onset of the erysipeloid skin lesion, he experienced abdominal pain which became localized in the right lower quadrant.

In retrospect, it was postulated that he had a perforated appendix, masked by the acute skin lesion. The subsequent course bears this out, and at operation, Aug 7, 1945, an inflammatory mass due to an old abscess was found, and remnants of the appendix with the coproliths were also removed. On Aug 11, a secondary closure of the wound was done. The postoperative course was uneventful and the patient was discharged to duty on Nov 28, eight months after first entering the sickbay.

Histologically, the remnants of the appendix showed evidence of chronic inflammation. The two coproliths consisted of hard shells of calcium salts around a nidus of fecal material, cellular debris, and inspissated mucus.

CASE IV J Q P, 56 year old retired business man was first seen by Dr Dwight L Wilbur on March 8, 1938, for a general check up. His symptoms were vague and referable to practically every organ system but his greatest concern was about his



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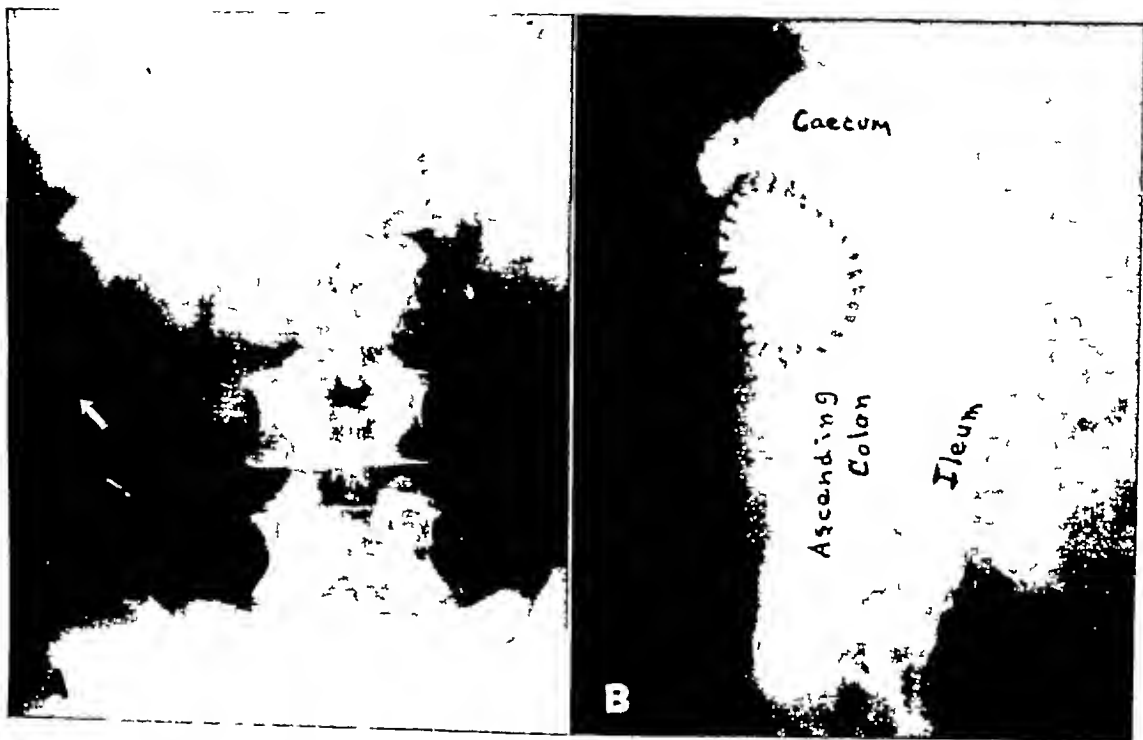


Fig 4 Case IV A A large, oval, 3×1.5 -cm laminated cigar shaped coprolith is seen high in the right side of the abdomen

B Six-hour examination made during a gastro-intestinal series demonstrates the malrotation of the cecum and the relationship of the cecum and ascending colon to the large coprolith

transfusion was done on Sept 9, and iron was given orally thereafter, because of a moderate anemia. The child improved rapidly, and on the twenty-second day of hospitalization (Sept 17) she was discharged to the out patient department.

The patient was followed bi-weekly until Nov 30, 1942 when she re entered the hospital for an interval appendectomy. Her only complaint then was intermittent pain in the lower abdomen and legs. Physical examination revealed no positive findings, and the blood count and urine were normal. A barium enema on Dec 4 revealed a "fecalith" in the appendix (Fig 5). Operation was done the following day. The tip of the appendix was adherent to the terminal ileum, and a fecalith could be felt in the mid portion. The appendix was removed. On pathological (and radiological) examination of the specimen, a firm (but crushable) fecalith was felt and seen in the mid portion, measuring $1 \times 0.7 \times 0.5$ cm. On cut section (and by x ray) an irregular laminated pattern of calcium was observed in the fecalith (Fig 5). The mucosa that remained (about two thirds of the circumference) over the fecalith showed fresh hemorrhage, and the appendiceal wall was infiltrated with lymphocytes. There were marked fibrosis of the submucosa and hypertrophy of the muscular wall. In other words the appendix showed real evidence of chronic inflammation and hypertrophy.

CASE VI R. M., a 13-year old boy, entered the hospital on Dec 9, 1945, complaining of pain in the right lower quadrant for six hours, which was sudden in onset. Actually, the pain originated in the right upper abdomen and radiated down into the right leg. There was no nausea, dysuria, diarrhea, or constipation. The temperature was 102° , pulse 88. On physical examination the abdomen was normal, but the right thigh was tender. There was limitation of motion of the right thigh and spasm of the muscles (rectus femoris and adductor group). Reflexes were intact and equal. Several blood studies revealed no leukocytosis (5,250-9,000 white cells with a normal distribution), the sedimentation rate was 16 mm/hr. The urine was negative.

Because of the indefinite pain in the leg, it was felt that spinal cord irritation should be ruled out, and a lumbar puncture was done. The spinal fluid was negative. The following day, on further questioning, a history of vague bouts of right lower quadrant pain was brought to light.

A series of roentgenograms were taken of the right hip. The bones of the pelvis and hips were negative, but it was noted that there was an opacity in the lower right quadrant that remained in constant relationship to the gas in the cecum (Fig 6). An appendiceal coprolith was suggested. The patient

³ This is described as a sign of appendicitis (21)



Fig 3 C A barium enema study shows the medial displacement of the cecum and its relationship to the opacities. A barium enema study done after operation showed that there was still slight displacement of the cecum but the opacities were gone. The displacement of the cecum was due to a large inflammatory mass.

blood pressure, which had been 170 mm Hg three years before. His prominent complaint, other than nervousness, irritability, and apprehension, was "a rumbling sensation and gas in the stomach." Examinations revealed a well preserved man for his years but no positive physical findings. Laboratory studies including urine and blood examination were not unusual. ECG changes suggested minimal myocardial damage.

On May 13, the patient complained of bouts of gas, but this was only one of a myriad of complaints. A barium enema and gastro intestinal series revealed a large coprolith in the right upper quadrant adjacent to the hyperrotated cecum (Fig 4) but because he was such a complainer, it was deemed wise not to mention this to the patient at the time.

On Aug. 10, there was a sudden onset of pain in the right side of the abdomen. This persisted for forty-eight hours and was described by the patient's physician as a typical severe attack of appendicitis with high fever (103°) and rather diffuse physical findings in the right side of the abdomen. No masses were palpable. A diagnosis of acute appendicitis was made, and at operation the physician found a large mass in the right upper quadrant. The entire mass, which included the terminal ileum, cecum, and appendix, was freed and left on the ab-

dominal wall. A diagnosis of carcinoma of the cecum was made on gross inspection.

The following day Dr. Emile Holman was called for removal of the exteriorized loop. He resected the mass and with it a portion of the terminal ileum, cecum, and appendix, and performed a side-to-end anastomosis of the ileum and ascending colon. The patient was slow to get back on his feet, but his post-operative course was not unusual.

The true nature of the mass was not appreciated until the specimen was opened by Dr. David A. Wood, and a large 3.0 X 1.5-cm appendiceal coprolith was found in an abscess contiguous to the perforated, dilated appendix. The inflammatory nature of the whole mass became apparent, and macroscopically no evidence of malignancy was found. The wall of the appendix was thicker than normal due to an increase in the muscular layer as well as to infiltration with leukocytes.

CASE V D A, a 6-year-old girl, was brought to San Francisco Hospital on Aug. 27, 1942, by her mother, who said that the patient had been vomiting for six days. On Aug. 21, she had a sudden lower abdominal pain. No nausea or vomiting ensued. The next morning, because she had no bowel movement, her mother gave her castor oil, milk of magnesia, and "green pills" without visible results. The following day the child started to vomit, the pain and obstipation persisted. She was believed to be "feverish" for at least two days.

On physical examination, the patient appeared apprehensive, lying on her right side, doubled up, complaining of a "stomach-ache." Her temperature was 101.4°, pulse 128, respirations 28, blood pressure 110/60. The skin was hot and dry. Examination of the chest revealed no dullness or rales. The heart showed no abnormalities. The abdomen was tense, with a firm mass filling the entire right lower quadrant and extending beyond the mid line to the left. Rectal examination disclosed a large, boggy, tender mass in the mid line.

Blood studies showed 70 per cent hemoglobin and a white cell count of 17,000 with 78 per cent neutrophils, 10 per cent of which were banded forms. The urine was negative. An x-ray examination of the abdomen revealed a large soft tissue mass filling the pelvic space.

Impression: Acute appendicitis with perforation and a pelvic abscess.

The patient was treated with fluids parenterally and hot compresses to the lower abdomen and kept in a high Fowler's position. For two days she was observed and parenteral fluid administration was continued. On Aug. 29 the pelvic mass had become fluctuant. An abscess was drained rectally, yielding 350 cc of pus in which the predominant organism was *E. coli*. A Penrose drain was left in the abscess for two days. Sulfathiazole was given and the temperature began to fall, reaching normal four days later when treatment was stopped. A

recovered from the acute episode quickly and was discharged. He returned to the out-patient department on Dec 31 and reported being well since his discharge. He was brought into the hospital for operation (appendectomy) on Jan 25, 1946. A normal appearing appendix was removed, containing an oval, hard concretion near the tip, with a smaller and softer "fecalith" palpable in the lumen (Fig 6). The postoperative course was not remarkable, and the boy was discharged well on Feb 7.

Histologically the wall of the appendix was thick, due to hypertrophy of the musculature, and there was infiltration of the wall with lymphocytes.

COMMENT

While the roentgenographic demonstration of coproliths in the appendix is not new (9, 11, 12, 13, 15, 22, 23, 24), the significance of the opacities in the right lower quadrant is brought to the attention of the radiologist, especially as an aid in the diagnosis of appendicitis in patients with recurrent attacks of right lower quadrant pain. In turn, the recognition of the significance of the opacities should lead to operative removal (13, 14, 25, 26) and a decrease in the morbidity (or even mortality) of this ubiquitous disease. This is doubly emphasized by a review of Case III, where the history of appendicitis was brought out only after the radiologist pointed out the appendiceal coproliths. Note should also be taken of the great length of the patient's incapacitating illness—eight months. The importance of removal of these coproliths is further demonstrated by Case IV, in which the physician, in spite of his knowledge that a large calculus was present, did not suggest its removal, and only after an acute attack of inflammation of the appendix with rupture was operation done.

Inferentially, then, it is more important to remove an appendix containing stones than it is to remove a gallbladder containing stones, as rupture of the appendix is imminent, while rupture is an unusual complication of gallbladder disease.

The amount of calcium and the degree of hardness of the calculus are undoubtedly dependent upon the age of the fecalith. In Case V, in a patient only six years old, the amount of calcium was very small.

It is estimated as being approximately the smallest amount demonstrable roentgenographically, even in a very thin person, and would be completely lost in an adult of normal weight (thickness). Kelly (27) reported a well developed concretion in a child of three and a half years of age. In Case IV the amount of calcium was large and the stone tremendous, being almost as large as any yet reported (29). In Case I the calculus was remarkable for its hardness, as it could not be crushed with a clamp, and it, too, was very opaque and laminated and must certainly have been many years old.

The origin and pathology of these coproliths have not been discussed here, as the subject has been well covered in many texts on appendicitis (27, 30, 31). The first mention of an appendiceal coprolith was in 1813 by Wegeler (32), who likened the concretions to gallstones.

One of the points emphasized by Pilcher (29) is the hypertrophy of the muscle wall of the appendix, which was noted in five of our six cases. This has not been brought out before and may be the mechanism of the intermittent colic, the history of which can be elicited after the presence of the calculus is discovered (Cases II, III, and VI). Shahan (25), in his case, also mentions "thickening" of the appendix, which contained 23 "hard stones." His patient recovered completely, symptomatically, following removal of the stone-filled appendix.

Since the inception of this paper, the diagnosis of appendiceal coproliths has been made an additional 8 times, with 2 more proved cases. One patient had had numerous bouts of abdominal pain with no recurrence of pain postoperatively to date (two months). The other patient entered in a very poor condition and the coprolith could be seen in a soft-tissue density which displaced the gas-filled bowel out of the right iliac fossa and ultimately proved to be a large abscess secondary to a ruptured appendix. Two of the most recent cases were similar to those reported by Seelig (15) and Mascherpa



Fig 5 Case V The after evacuation barium enema film shows the appendix partially filled The barium ends in a curvilinear shadow and below this a faint opacity can be seen A roentgenogram of the specimen demonstrates the beginning laminated pattern of the incomplete calcification of the fecalith

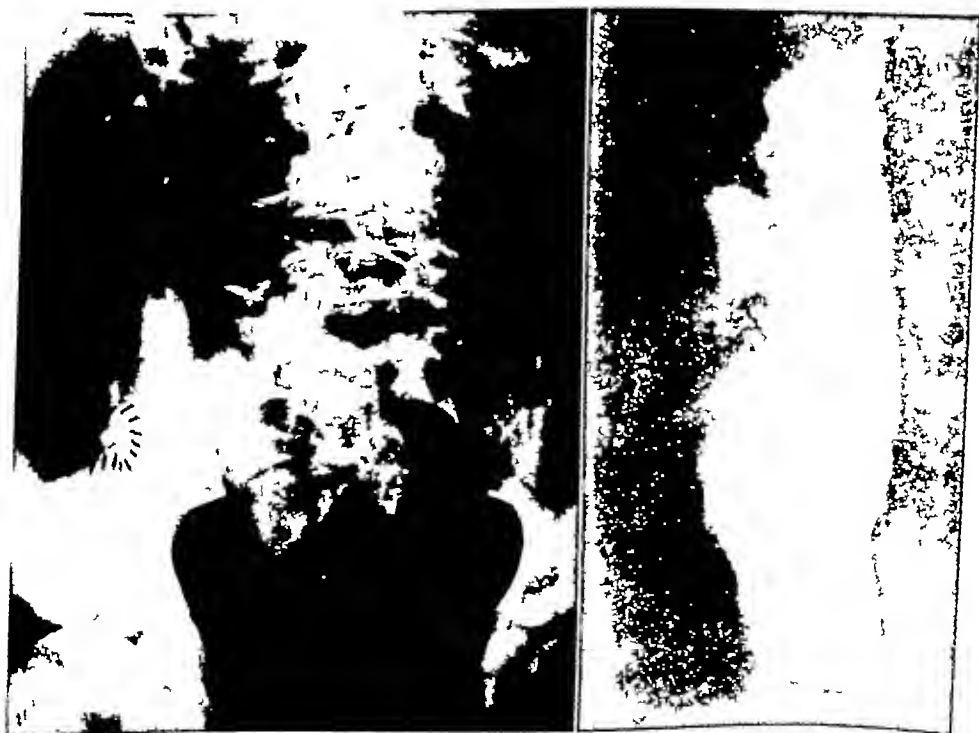


Fig 6 Case VI The dense coprolith can be seen in the right lower quadrant This remained in constant relation to the gas filled cecum A roentgenogram of the specimen demonstrates the density of the opacity and one other fecalith in the tip which contains calcium but this one could not be seen in the roentgenogram of the abdomen

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(17), as the presenting symptoms were referable to the urinary tract

This is not an attempt to popularize the needless operation for the impossible roentgen diagnosis of chronic appendicitis, but it is an attempt to explain on a mechanical basis one of the causes of complications of appendicitis and to show that, although the roentgenologic diagnosis of chronic appendicitis has proved unsatisfactory even in the best of hands (26), a number of patients may be saved the needless chance of an attack of appendicitis with the complications herein reported

SUMMARY

1 The importance of the diagnosis of appendiceal coproliths is emphasized, especially since it is believed that such a diagnosis warrants operative intervention

2 Six cases of appendiceal coproliths are reported, in four of which the seriousness of the disease following rupture of the appendix is exemplified

3 One of the four largest coproliths yet reported—30 × 15 cm—is included in this small series

4 When the diagnosis of "chronic appendicitis" is entertained, a roentgenogram of the abdomen with the patient supine should be made to rule out the possibility of a calcified appendiceal coprolith. But one must remember that the diagnosis of chronic appendicitis is impossible roentgenographically. It is only inferred that, when a clear-cut history fits with the roentgenographic diagnosis of an appendiceal coprolith, operation for chronic recurring appendicitis will yield benefits

Palo Alto Clinic
Palo Alto, Calif

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DISCUSSION

John H Camp, M D (Rochester, Minn) Dr Thomas referred or said someone referred to this subject as old stuff Perhaps it is, but the older one gets in the practice of medicine, the more he realizes that there isn't so much that is actually new, anyway If we go back far enough in the old literature, especially in Virchow's *Archives*, we frequently find things that some of us get excited about these days because they appear new Nevertheless, many of them take on increased significance because of advances in diagnosis and the increase in our knowledge of various clinical phenomena

I was fortunate enough to have Dr Thomas as one of my assistants during my Navy career, and our experience in seeing a few cases of appendiceal coproliths emphasized, at least to me, the importance of these shadows in the lower right quadrant

I am sure that Dr Thomas doesn't want to leave with you the idea that the presence of such a shadow justifies a diagnosis of appendicitis on the part of the radiologist Rather, I think it should emphasize that in a patient who is having recurrent right lower quadrant symptoms we should seriously consider appendiceal disease and the surgeon should be on the alert for the discovery of the condition and its complications

The presence of coproliths in the appendix is important because, as these cases emphasize, when the patients are allowed to continue with recurrent attacks of appendicitis, serious complications may result If we can help avoid these by contributing this little roentgenologic bit, I think this review of so-called "old stuff" has justified itself

Paul C Swenson (Philadelphia, Penna) I would like to ask Dr Thomas one question Has he found the origin for the calcium in these lumps?

Dr Thomas (*closing*) Dr Swenson has asked concerning the formation of the coproliths It is believed that their formation may be similar to that described by Phemister *et al* in the *Annals of Surgery*, in October 1931 and 1932 In these articles, it is postulated that stones of high calcium carbonate content are formed only after obstruction of the gallbladder Because most of the appendiceal coproliths contain a high percentage of calcium carbonate, the same mechanism probably exists

SUMARIO

Coprolitos Apendiculares Su Importancia Quirúrgica

Recálcase la importancia del diagnóstico de los coprolitos apendiculares, en particular por creerse que ese diagnóstico justifica la intervención cruenta

Comunicanse seis casos, en 4 de los cuales pónese de manifiesto la gravedad del estado cuando sobreviene perforación del apéndice Esta pequeña serie comprende uno de los 4 mayores coprolitos descritos hasta ahora 3.0 X 1.5 cm

Cuando se considera el diagnóstico de

"apendicitis crónica," debe hacerse una radiografía del abdomen con el enfermo en posición supina, a fin de excluir la posibilidad de coprolitos apendiculares calcificados, pero recordando la imposibilidad de hacer roentgenográficamente el diagnóstico de la apendicitis crónica Sólo cabe colegir que, cuando una historia bien definida concuerda con el diagnóstico radiográfico de coprolito apendicular, resultará beneficiosa una operación por apendicitis recurrente crónica

Problems in the Diagnosis of Cancer of the Colon¹

KENNETH S DAVIS, M D, and WILLIAM H DANIEL, M D

Los Angeles, Calif.

WE CANNOT view with complacency the fact that almost a year has elapsed before the average patient with cancer of the colon has an accurate diagnosis made. Furthermore, there are no symptoms which can be designated as distinctive of a malignant growth of the colon, these varying widely, depending on the location and the gross form of the tumor and on the presence or absence of complicating factors such as ulceration, perforation, obstruction, secondary infection, and hemorrhage.

The colon is the site of many other pathological processes which resemble cancer in their clinical and roentgenologic manifestations. Many patients are operated on for appendicitis only to have a cancer in the proximal colon disclosed. Ileocecal tuberculosis and regional enteritis may also simulate carcinoma. In the distal colon, diverticulitis, especially with an inflammatory mass, often cannot be differentiated from cancer. In the rectum, operations are frequently done for hemorrhoids only to have a cancer disclosed at a later date.

SYMPTOMS

Cancer of the Colon According to Rankin, it is impossible to correlate symptoms and signs referable to the entire colon as if it were a single organ, because of the wide differences in the proximal and distal portions, both structurally and functionally. On his basis of symptomatology, cancer in the proximal colon may be divided into three groups: (1) the dyspeptic group, usually diagnosed as chronic appendicitis or cholecystitis, (2) the group characterized by unexplained anemia and weakness, (3) the group in which a tumor is discovered accidentally, or in the course of a routine examination. Twenty-six

per cent of carcinomas of the cecum and ascending colon falling in Group 1 were diagnosed as appendicitis, 90 per cent of these patients complained of pain and soreness in the lower right quadrant of the abdomen from two to nine months before exploratory operation. In Group 2, the weakness and anemia are not accompanied by visible bleeding from the rectum. It is in this group that a thorough roentgenographic study is indicated, not only of the colon but of the entire gastro-intestinal tract.

In the distal colon, obstructive phenomena dominate the clinical picture, since cancers in this region tend to be encircling in type, causing progressive stenosis. Furthermore, the fecal content in the left half of the colon is hard and formed and can be forced only with difficulty through a closing segment. A history of progressive constipation can be obtained in from 50 to 60 per cent of these cases.

In acute obstruction of the colon, the symptoms are very similar to those of small bowel obstruction, with marked abdominal distention and evidence of hyperactive peristalsis. In these cases a "scout" roentgenogram of the abdomen is indicated, as it will aid materially in localizing the point of obstruction.

The appearance of bright or dark red blood in the stool, especially if it persists on repeated examinations, suggests the possibility of a cancer distal to the splenic flexure of the colon. Lesions in the proximal colon seldom cause bleeding, if they do, the blood is dark in color and tarry in consistency.

Cancer of the Rectum and Rectosigmoid Cancers of the rectum may cause early symptoms, but in a majority of cases the

¹ Presented at the Thirty second Annual Meeting of the Radiological Society of North America Chicago Ill Dec 1-6, 1946

patient either disregards them or they are misinterpreted. The average duration of symptoms before diagnosis, as given by Rankin, is approximately twelve months. The most frequently encountered symptoms are bleeding and changes in bowel habit, frequent desire to stool, often mistaken for diarrhea, with the passage of blood or mucus, predominates. Loss of weight and strength are worthless symptoms in the early recognition of the condition. To wait for the so-called textbook symptoms to appear, as anemia, loss of weight and strength, palpable mass, etc., is merely to postpone the diagnosis until there is no hope for cure.

DIAGNOSIS

Diagnostic errors in the recognition of cancer of the colon are both of omission and commission. Failure to make a proper examination results in more errors in diagnosis than any other factor. The first point of examination should be the rectum and sigmoid colon, since the majority of cancers of the colon are found in these areas. Seventy-five per cent of cancers of the rectum are within reach of the examining finger, the remainder can usually be visualized through the proctoscope. The digital and the proctoscopic examination should always precede the roentgenological study. Palpation of the rectum should be done in the left lateral position, it is followed by sigmoidoscopic examination in the inverted position if the instrument cannot be passed the desired length while the patient is lying on the side.

If a definite advanced lesion is found by palpation and visualized through the instrument, x-ray examination is usually unnecessary. If the lesion is annular and obstructing, the use of the barium enema is contraindicated, since a partial obstruction may be converted into a complete one by the barium.

If a non-obstructing lesion is seen by the proctologist and symptoms of obstruction are present, a barium enema study should be done, as it may show a second lesion in

another segment of the colon, multiple growths being not uncommon. The barium enema should always precede the oral meal for two reasons. (1) Barium by mouth is dangerous in the presence of an obstructing lesion and may produce an acute obstruction. (2) The motor meal study is of far less value in ruling out an organic lesion, owing to the irregular distribution of the barium throughout the lumen of the colon.

If one or more polyps are found in the proctoscopic study, the air-contrast barium enema as employed by Weber is essential, since polyps are often multiple.

If blood is a constant finding in repeated examinations with the sigmoidoscope and all local causes are ruled out, the plain barium enema followed by an air-contrast study is essential. This should be repeated several times if the findings are negative or indeterminate. In the event that no lesion is demonstrated by the x-ray and blood continues to be present, an exploratory operation is justified.

The sigmoid colon can well be termed the silent area of the gastro-intestinal tract, as it frequently drops downward behind the upper rectum and in some instances cannot be visualized, regardless of the position of the patient. The enema may pass through a lesion without obstruction and the lesion not be seen. Furthermore, a tumor in the sigmoid may intussuscept into the upper rectum and not be revealed by the barium enema although readily seen through the proctoscope.

Frequent sigmoidoscopic examinations are helpful in differentiating between malignant and inflammatory lesions, especially in the presence of diverticulitis, where the roentgen findings are indeterminate. Bleeding from a diverticulitis is rare, whereas the constant appearance of blood points to cancer.

DIFFERENTIAL DIAGNOSIS

Cancer of the colon accounts for about 70 per cent of required operations on the colon, so that it would seem advisable to consider a malignant growth in the differ-

Problems in the Diagnosis of Cancer of the Colon¹

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David G Pugh, M D (Rochester, Minn.) Dr Davis has ably discussed many problems that are encountered in the diagnosis of carcinoma of the colon. I am especially pleased that he recommended the proctosigmoidoscopic examination as an adjunct to the roentgenologic examination of the colon. The proctosigmoidoscopic examination is the best method of diagnosing lesions of the rectum and rectosigmoid and it is especially valuable in the recognition of inflammatory diseases of the colon if the lower segments are involved. If at all possible, this examination should precede the roentgen examination. Under such circumstances the roentgenologist will need to be concerned only with that part of the colon that is above the proctologist's vision.

If a proctosigmoidoscopic examination is not obtainable, it is necessary to examine the entire colon, including the lower segments, by roentgenologic methods. By use of the customary roentgenologic technic all of the colon that can be palpated—and that includes all but the rectum, rectosigmoid, and varying lengths of the sigmoid—can be satisfactorily examined. In order to examine those lower seg-

ments, a double-contrast study must be done. Ordinarily double-contrast studies of the rectum and lower part of the sigmoid are not satisfactory when the upper part of the colon is also examined, since too much fluid remains in the bowel after efforts at evacuation and often there is barium mixture in the terminal ileum. It is therefore usually necessary that a localized air study of the lower part of the colon be done a day or so later. In this way an excellent roentgenologic view of this segment of the bowel can be obtained, but this does not approach the degree of accuracy that is obtained by a proctosigmoidoscopic examination. It seems to me, therefore, that a combination of proctosigmoidoscopic and roentgenologic examination is ideal if a complete study of the colon is desired.

Kenneth S Davis, M D (*closing*) There is one point I failed to mention in my paper. That is, before we give any barium at all by mouth, for whatever reasons, we always take a scout roentgenogram of the abdomen to see if there is any distention with gas. In the presence of an excessive amount of gas we do not give barium by mouth.

SUMARIO

Problemas Planteados por el Diagnóstico del Cáncer del Colon

En la exploración corriente del colon, el examen digital debe ser lo primero, pues 75 por ciento de los cánceres del recto son accesibles al dedo explorador. Luego debe venir el estudio sigmoidoscópico. Si este examen revela una lesión avanzada, el estudio roentgenológico suele resultar innecesario.

El enema de bario debe preceder siempre al bario por vía oral, pues el último es peligroso si existen lesiones obstructoras. Si los hallazgos radiológicos no son termi-

nantes o si persisten los síntomas, hay que repetir el examen.

Si la proctoscopia revela uno o más pólipos, debe ejecutarse un estudio con el neumo-enema de bario de contraste, que emplea Weber, dado que los pólipos son a menudo múltiples.

Si se encuentra hemorragia persistente en exámenes sigmoidoscópicos repetidos, está indicada una operación exploradora a pesar de los hallazgos roentgenológicos negativos.



ential diagnosis unless it can be conclusively proved otherwise

In the proximal colon, appendiceal abscess, hyperplastic ileocecal tuberculosis, actinomycosis, regional enteritis, and intussusception must be differentiated from carcinoma

In the distal colon, the filling defect produced by diverticulitis more closely simulates cancer than any other lesion, the filling defect may be due to persistent spasticity or be a true defect resulting from encroachment on the lumen of the bowel by pericolic inflammatory tissue. The differentiation is rendered more difficult with the presence of diverticula elsewhere in the colon

In chronic ulcerative colitis, the proctoscopic examination, if done by an experienced proctologist, gives the most important data for diagnosis

Sigmoidoscopic examination should be the rule in cases with symptoms suggesting colitis or dysentery, to exclude carcinoma. This should be followed by the barium enema study. Segmental chronic ulcerative colitis may produce the classic roentgen findings of carcinoma, namely obstruction, filling defect, and palpable mass.

In polyposis of the colon, one should always keep in mind the high incidence of malignant change, especially in cases of diffuse polyposis, and radical surgical treatment should be considered in these cases

CONCLUSIONS

In the routine examination of the colon, the digital examination should be first, as 75 per cent of cancers of the rectum can be reached by the examining finger. This should be followed by the sigmoidoscopic study. If an advanced lesion is found in this examination, the x-ray study is usually unnecessary.

The barium enema should always precede oral administration of barium, since barium by mouth is dangerous if obstructing lesions are present. If the roentgen findings are not conclusive or if there is a

persistence of symptoms, the examination should be repeated

If one or more polyps are found in the proctoscopic study, an air-contrast barium enema study as employed by Weber should be done, since polyps are often multiple

If persistent bleeding is found in repeated sigmoidoscopic examinations, surgical exploration is indicated despite negative roentgen findings

2131 West 3d St
Los Angeles 5 Calif

DISCUSSION

Maurice Feldman, M.D. (Baltimore, Md.) A survey of the statistics on failure to diagnose cancer of the colon is not available at the present time. Errors in the roentgen diagnosis, however, are common to all roentgenologists. Our goal should be to keep these errors to a minimum.

It is noteworthy that at times the roentgen examination of the colon is misleading and for that reason one should not neglect the clinical observations and proctoscopic, sigmoidoscopic, and stool examinations in any case of suspected colonic disease.

The roentgen diagnosis of carcinoma of the colon presents many pitfalls, which Dr. Davis and Dr. Daniel have well outlined. Early and even moderately late cases of carcinoma of the colon may be overlooked or obscured as a result, first, of the site of the lesion, second, over-filling of the area involved, third, overlapping of loops of bowel, fourth, a minimal lesion, fifth, the pathologic type of carcinoma.

To obtain the best diagnostic result the following measures must be utilized:

First, use as thin a barium solution as is possible.

Second, observe the flow of the opaque medium carefully under the fluoroscope.

Third, study the colon in the prone, supine, and oblique positions.

Fourth, look upon any area of incomplete filling or segmental emptying with suspicion.

Fifth, repeat the colon enema in all suspected cases.

Sixth, correlate the clinical manifestations.

Seventh, in all cases of blood in the stools, either occult or visible, where the source in the upper tract has been eliminated, repeated study of the colon is not only necessary but imperative.

I might suggest that the colonic roentgen study be planned in two stages, especially for examination of the lower colon, the rectum, and sigmoid. The first stage is to fill the rectum and partially fill the sigmoid and take a series of films of the rectum and sigmoid only. In the second type, the colon is completely filled. This procedure will eliminate over-shadowing of redundant loops of colon, and over-shadowing of the terminal ileum.



Fig 1 A Admission roentgenogram showing osteoblastic metastases involving the lumbar spine, sacrum, pelvis and upper ends of the femurs
 B Roentgenogram of same patient five months after institution of stilbestrol treatment showing a notable decrease in the number and density of the metastatic areas

and pelvis, separately or in conjunction with intravenous pyelograms, revealed osseous metastases in 29 patients. The predominant type of bone involvement was osteoblastic. In only 2 cases were true osteolytic metastatic lesions demonstrable.

Of the 29 patients showing osseous metastases, 6 were treated by orchiectomy alone, 21 had orchiectomy plus stilbestrol therapy, and 2 were given stilbestrol without castration. Transurethral resection was required in 11 of these cases, while 10 had x-ray therapy either before or after admission for treatment.

Table I outlines the changes noted in the appearance of the osseous metastases following estrogenic therapy. In 3 patients, demonstrable osseous metastases developed some time after estrogenic therapy had been instituted (ten months, sixteen months, two months). In 2 instances, there was no notable change in the appearance of the metastatic areas at follow-up examination. In 4 cases the

TABLE I X RAY CHANGES IN METASTASES FOLLOWING ORCHIECTOMY AND/OR STILBESTROL THERAPY

Metastases developed	3
No change in metastases	2
Metastases progressed unchanged in character	4
Metastases become more discrete	5
Improved	2
Improved but recurred	1
Disappeared	2
No follow up	10
TOTAL	29

osseous metastases progressed unchanged in spite of therapy, in 5 they became more dense and more discrete.

The follow-up roentgenograms in 2 cases showed definite improvement, evidenced by a diminution in the amount of involvement of the bone. The original configuration of the metastatic area, however, had not changed in character. Figure 1 is an illustration of such a case. The patient was a 74-year-old male who was admitted to the hospital in March 1944, because of vomiting. The clinical diagnosis was carcinoma of the prostate. Roentgenograms

Effects of Estrogenic Therapy¹ on Osseous Metastases from Carcinoma of the Prostate

WILLIAM C. MACCARTY, JR., M.D.

Associate Radiologist, The Hitchcock Clinic, Hanover, N. H.

THE INCREASING role played by hormonal therapy in the treatment of certain types of malignant growth, especially carcinoma of the female and male breasts and of the prostate gland, has prompted this study. Huggins (1), in his original report on orchiectomy as a method of treatment for carcinoma of the prostate, noted that 15 of his 21 patients who had been treated by orchiectomy had osseous metastases. Of these, he states "In all cases in which metastases were present, which were followed for long periods, increased osteosclerosis of the metastases was observed within three to six months after castration." Nesbit and Cummings (2) review the results obtained by orchiectomy in 75 patients with carcinoma of the prostate, of whom 31 had osseous metastases. In 4 of 12 cases which were followed six months after orchiectomy, definite regression of the metastases was observed. Alyea and Henderson (3) report that "following castration there is a distinct smoothing and sclerosing of the bone detail, approaching more normal type of bone." Nathanson (4) states that bone metastases may no longer be visible by x-ray, following orchiectomy. Our experience during the past four years closely parallels the work of these investigators.

From 1942 to 1945, inclusive, 67 patients with carcinoma of the prostate gland were treated in the Mary Hitchcock Memorial Hospital. The basis for diagnosis was clinical evidence of the primary carcinoma, with or without osseous metastases, plus a positive biopsy in slightly over half of the cases. The oldest patient in the group was 87 years of age, the youngest

52 years, the average age was 69. The initial symptom in 43 cases was referable directly to the urinary tract. Eleven patients complained of pain of the skeletal type, usually in the pelvis or hips, in addition to the usual symptoms brought about by prostatic enlargement. Nine of the patients complained of bone pain as the only initial symptom. The remainder of the group presented themselves for reasons which at the time were not considered related to prostatic disease.

Biopsy specimens were obtained in all cases requiring transurethral resection for bladder neck obstruction. This procedure was carried out on 37 of the 67 patients. The diagnosis returned from the laboratory was adenocarcinoma in 35 instances and benign hypertrophied prostatic tissue in 2 patients. The latter report is understandable when one considers how little of the entire gland may be removed in alleviating bladder neck obstruction.

At the time this study was carried out, orchiectomy and/or stilbestrol therapy were the procedures of choice in treating carcinoma of the prostate. Orchiectomy was performed 51 times in this series. Most of these patients, in addition, had received stilbestrol prior to surgery or were discharged on a maintenance dose of the drug. Sixteen patients were treated with stilbestrol alone. Transurethral resection was necessary because of bladder neck obstruction in 37 of the entire group. In 13 instances, x-ray therapy had been instituted either prior to estrogenic therapy or was required subsequently to control pain.

Roentgenograms of the lumbar spine

¹ The words "estrogenic therapy" as used in this paper imply orchiectomy and/or the use of the drug stilbestrol.

² Accepted for publication in October 1946

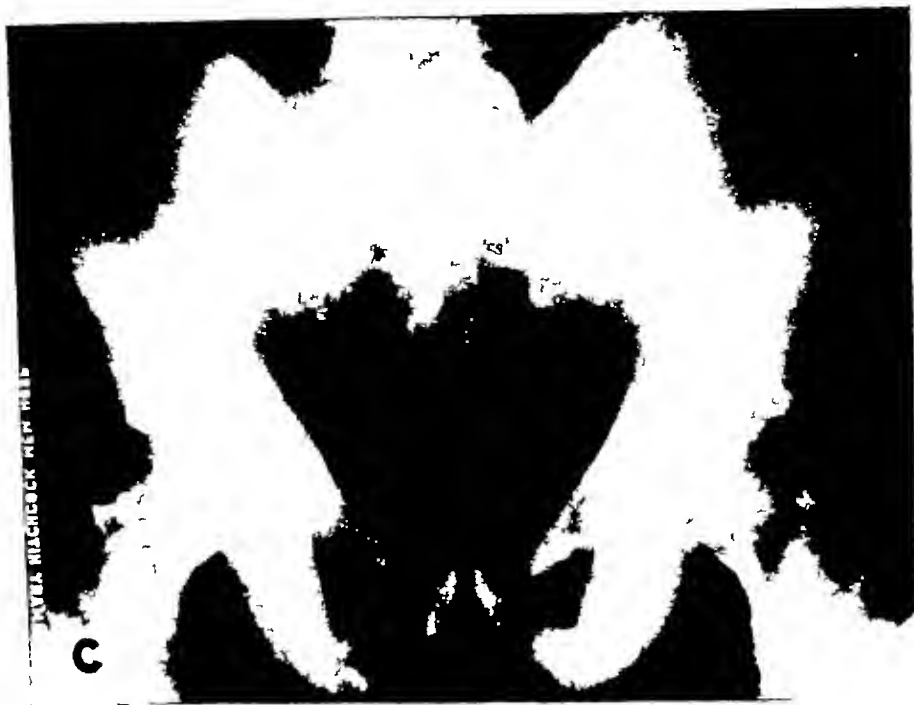


Fig 2 C Roentgenogram of patient shown in Figs 2A and 2B five months after the metastatic lesions had apparently disappeared. There are now extensive diffuse metastases throughout the entire pelvis.

revealed osteoblastic metastases in the pelvis and lumbar vertebrae (Fig 1A). Treatment was by stilbestrol alone, with excellent temporary clinical improvement lasting five months. An orchiectomy was performed in August 1944. In spite of temporary symptomatic relief and a noticeable improvement in the appearance of the osseous metastases (Fig 1B), the patient died in November 1944, eight months after treatment was instituted.

Figure 2 illustrates one of the most unusual changes observed in the metastatic processes and is the only such case in this series. The patient was a 70-year-old man in whose case a diagnosis of carcinoma of the prostate had been established elsewhere in 1941, following a transurethral resection. He had also received x-ray treatment for low back and pelvic pain. He was admitted to our hospital in 1942, complaining of dysuria. Roentgenograms (Fig 2A) revealed osteoblastic metastases. Orchiectomy was carried out and the patient was discharged on a maintenance dose of stilbestrol. Follow-up roentgeno-

grams revealed no change in the appearance of the metastases in May 1943, but in June 1944 they had practically disappeared (Fig 2B). When the patient was last seen in November 1944, however, he was failing rapidly, and extensive osteoblastic metastases of a different type from those seen originally were demonstrable (Fig 2C).

The most striking roentgenographic changes were noted in the two patients in whom we considered the bony metastases to have disappeared. The first of these patients was a 77-year-old male who was admitted in March 1942, with a dysuria of five years' duration. Roentgenograms (Fig 3A) in conjunction with an intravenous pyelogram revealed an osteolytic process in the left pubic bone. A bilateral orchiectomy was performed as the sole method of treatment. When the patient was last seen, in October 1943, nineteen months later, there had been a complete recalcification and filling in of the metastatic area (Fig 3B), and he was symptom-free.

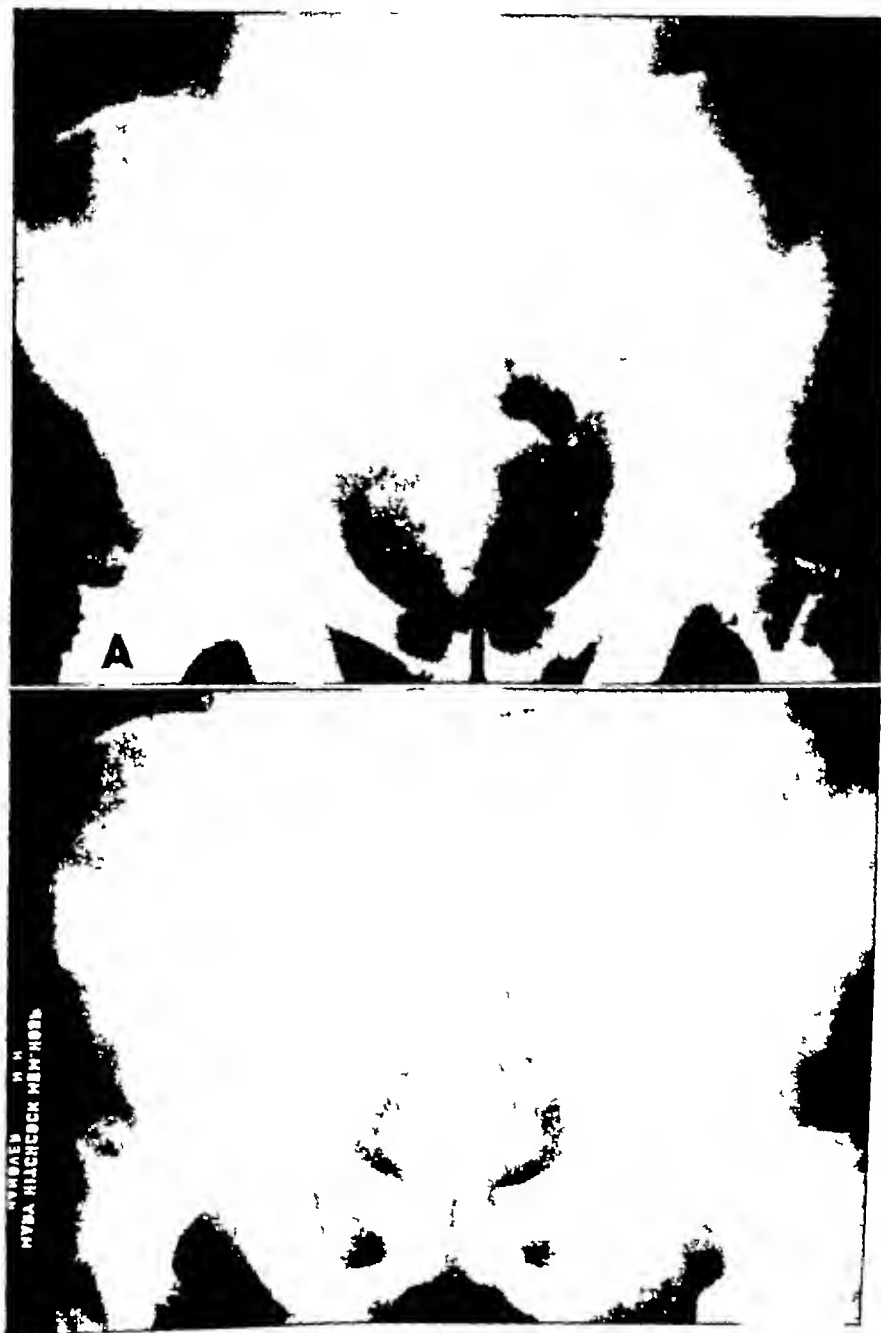


Fig 2 A Admission roentgenogram of a seventy year old man showing multiple rounded irregular areas of varying size throughout the pelvis representing osteoblastic metastases

B Roentgenogram of same patient twenty-two months after institution of estrogenic therapy revealing practically complete disappearance of the pelvic metastases See also Fig 2C



Fig 4 A and B Roentgenograms revealing extensive metastases involving particularly the bodies of the third and fourth lumbar vertebrae and the bones of the pelvis
 C and D Roentgenograms of the same patient taken eighteen months after orchiectomy and institution of stilbestrol therapy The osteoblastic metastases involving the vertebrae and pelvis have completely disappeared



Fig 3 A Osteolytic metastatic process completely destroying most of the left pubic bone
B Roentgenogram taken nineteen months after orchietomy showing complete recalcification and filling in of the metastatic area shown in A



Fig 4 A and B Roentgenograms revealing extensive metastases involving particularly the bodies of the third and fourth lumbar vertebrae and the bones of the pelvis

C and D Roentgenograms of the same patient taken eighteen months after orchiectomy and institution of stilbestrol therapy. The osteoblastic metastases involving the vertebrae and pelvis have completely disappeared

The second patient, in whom similar changes were noted, was a 50-year-old male who had had known carcinoma of the prostate for eight years. He had had four previous transurethral resections, the first in 1934, elsewhere, the second and third in our hospital in 1937 and 1938, respectively, and the fourth elsewhere in 1940. In each instance, a diagnosis of adenocarcinoma had been returned from the laboratory. The pathological sections obtained in 1934 were reviewed by our pathologist. Osteoblastic metastases were known to have been present since 1938. A series of x-ray treatments was directed over the pelvis in 1940. In November 1942, the patient was admitted again because of pain in the back and pelvis, as well as dysuria. Roentgenograms taken at the time showed osteoblastic metastases in the lumbar vertebrae and the pelvic bones (Fig 4 A and B). Orchiectomy was performed and the patient was discharged on stilbestrol therapy. Eight months later he returned for the removal of a bladder stone. No change was noted in the areas of osseous metastases. In May 1944, eighteen months after orchiectomy, roentgenograms (Fig 4 C and D) revealed complete disappearance of the metastatic areas. The patient has been seen repeatedly since that time. There has been no recurrence of the osseous metastases and he is clinically well, except for occasional attacks of cystitis, eleven years after the diagnosis was established and thirty-four months after orchiectomy.

Of the 29 patients with osseous metastases, 10 failed to return after their original visit to the hospital. The average duration of follow-up for the 19 who returned for check-up and further treatment was 14.2 months. The longest was 48 months.

Table II is a summary of the clinical results obtained in the entire series of 67 cases. It is noted that approximately one-third of the patients improved, one-third

TABLE II CLINICAL RESULTS OF TREATMENT OF PROSTATIC CARCINOMA

No follow up	26
Improved	24
Dead (includes cases which improved temporarily)	6
Temporary improvement only	5
Worse	4
No change	4

were not followed, and one-third were unaffected so far as the course of their disease was concerned.

SUMMARY

During a four-year period, 1942-45 inclusive, 67 patients with carcinoma of the prostate gland received estrogenic therapy. Twenty-nine of these patients had roentgenographic evidence of osseous metastases. Nineteen of the latter were followed over a period averaging 14.2 months. Unusual changes were observed in the osseous metastases, unlike those noted prior to estrogenic therapy. The characteristics of these alterations in the roentgenographic appearance of the osseous metastases have been described.

CONCLUSION

The radiologist in interpreting roentgenograms which demonstrate osseous metastases from carcinoma of the prostate should be familiar with the alterations in the bone lesions produced by estrogenic therapy.

Hitchcock Clinic
Hanover, N. H.

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SUMARIO

Efectos de la Estrogenoterapia sobre las Metástasis Oseas del Carcinoma Prostático

Durante un cuatrenio (1942-1946) 67 enfermos con carcinoma de la próstata fueron tratados con estrógeno. Veinte y nueve de esos enfermos tenían signos radiográficos de metástasis óseas, y 19 de éstos fueron observados durante un período subsiguiente que promedió 14.2 meses. En las metástasis notáronse alteraciones peculiares y distintas de las observadas antes de la estrogenoterapia.

En 5 casos las metástasis se volvieron más espesas y más discretas, en 2 hubo mejoría bien definida según reveló la dis-

minución de la cantidad de hueso invadido, aunque no se modificó la configuración primitiva de la zona metastática. En 1 caso las metástasis prácticamente desaparecieron, pero fueron seguidas de extensas metástasis osteoblásticas de un tipo distinto. En 2 casos la desaparición de las metástasis fué completa.

Al interpretar roentgenogramas que revelan metástasis óseas de un carcinoma prostático, el radiólogo debe estar familiarizado con las alteraciones que produce la estrogenoterapia en las lesiones óseas.



Irradiation of Experimental Cerebral Tumours¹

I Experimental Production of Brain Tumours in Mice

KATHARINE TANSLEY, D Sc ²

II Some Observations on the Effect of X-Radiation on Experimental Gliomata in Mice

KATHARINE TANSLEY, D Sc, and C W WILSON, M Sc, PhD, F Inst P ³

THE RESULTS of treatment of cerebral tumours by radiotherapy are generally admitted to be very unsatisfactory, although recently Peirce, Cone, Elvidge, and Tye (14) report rather more hopeful results. We have little knowledge of what types of cerebral tumour, if any, are suitable for radiotherapy (Bailey, 4, Bailey, Sosman, and Van Dessel, 5, Alpers and Pancoast, 1, Tarlov, 21). There is a good deal of evidence, also, that doses of x-rays or gamma rays likely to be effective in destroying a tumour have a destructive effect on brain tissue (Fischer and Holfelder, 8, Lyman, Kupalov, and Scholz, 11, Scholz, 17 and 18, Scholz and Hsu, 19, Markiewicz, 12, Wachowski and Chenaault, 22), as well as on the skull (Camp and Moreton, 7).

It seemed, therefore, that it would be useful to investigate the effects of radiation on experimental cerebral tumours in animals.

PART I

The production of cerebral tumours by the introduction of carcinogens into the brain tissue of experimental animals is not an entirely simple matter, the results vary according to the species and strain of animal, carcinogenic substance and technique used. Most of the earlier attempts were unsuccessful. Askanazy (2) claimed to have obtained chondrosarcomata in the rabbit cerebellum as a result of introducing benzpyrene in olive oil or beef fat, but his results are questioned by Zimmerman and Arnold (28), while Bertrand and Gruner (6) found no true gligenous neoplasia after

injecting benzpyrene in lanolin, paraffin oil, or vaseline into the brains of rabbits. Weil (23), working on rats, appears to have been the first to obtain undemable gliomata. He used crystalline dibenzanthracene in cholesterol, as well as styryl 430 in saline, with the former he obtained one invasive tumour among many failures, but with the latter he was usually able to induce tumours resembling human glioblastomata or meningiomata depending on the site of origin. Seligman and Shear (20) failed to produce gliomata in rats, mice, cats, or guinea-pigs by brain injections of methylcholanthrene in various media, but succeeded with mice when the carcinogen was introduced in the form of pellets, a result which was confirmed by Peers (13) who, however, got negative results in rats and rabbits when he used benzpyrene either in the solid form or dissolved in various media. Zimmerman and Arnold (3, 25-29), in an extensive investigation, have produced sarcomata and gliomata of various types in the brains of some pure strains of mice by the use of methylcholanthrene, benzpyrene, and dibenzanthracene pellets. These tumours could be preserved through several generations of host animals by grafting them under the skin of the back, as well as into the anterior chamber of the eye (Freeman and Zimmerman, 9). Later Russell (16) obtained cerebral tumours in rats by the use of pellets composed of a mixture of cholesterol and methylcholanthrene, and Lopez (10) produced a cerebral glioma by feeding a rat with 2-acetyl-aminofluorene.

In the present investigation, attempts to

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² Sir Halley Stewart Fellow. Strangeways Research Laboratory, Cambridge, England. Now at the Physiology Department, Birmingham University.

³ Physics Department, Westminster Hospital, London, England.

produce cerebral tumours in mice by the introduction of benzpyrene powder resulted in two sarcomata in a total of 131 animals, benzpyrene pellets made according to the method described by Zimmerman and Arnold (28) produced no tumours in 13 animals, and methylcholanthrene pellets have, at the time of writing (339 days after the implantation) produced one sarcoma among 31 animals. The introduction of methylcholanthrene powder has been much more successful, 24 sarcomata and 10 gliomata having been obtained in 77 animals. The present paper deals only with the experiments in which methylcholanthrene powder was used.

Owing to experimental difficulties, which will be described later, only one glioma was preserved by transplantation, but this has now been transmitted to 103 mice, 49 of which have been subjected to x-ray irradiation.

Method Two strains of mice were used for the production of the induced tumours, the albino N₁ strain, originally obtained from the National Institute for Medical Research, London, and a mixed pigmented stock of uncertain origin bred in the laboratory. For the subsequent grafting of the tumours the N₁ strain only was used.

The operation of implanting the carcinogen was performed when the mice were two days old. Under ether anaesthesia a central incision from the level of the shoulders to that of the eyes was made in the skin. A semicircular flap was then cut in the skull with a small scalpel, and the methylcholanthrene powder (Hoffmann-LaRoche) was injected into the left hemisphere. For this the point of a wide gauge hypodermic needle was cut off and a small amount of the powdered methylcholanthrene pressed into the tip, a special metal plunger was used to push the methylcholanthrene deep into the brain tissue after the needle had been inserted into the hemisphere. The skull flap was then allowed to drop back into position and the edges of the skin were fastened together with 2 per cent celloidin solution. The animals were allowed to recover from

the anaesthetic in an incubator at 37° C before being returned to their mothers. Aseptic precautions were, as far as possible, observed throughout the operation.

The glioma used for grafting was obtained from an animal 397 days after the implantation of methylcholanthrene. The mouse was killed with chloroform and the brain was removed and cut open. Part of the left hemisphere, which showed many small haemorrhages, was cut out and placed in sterile saline, while the rest of the brain was fixed in Zenker's solution. The brain tissue to be grafted was then cut into small pieces and these were implanted in the brains of a litter of 2-day-old mice. The method was similar to that used for the original implantation of methylcholanthrene except that a piece of tissue was cut out of the left hemisphere and the fragment of tumour placed in the hole so formed.

The grafted tumour fragments produced marked lumps on the heads of the host mice, and these were measured daily with calipers as soon as they were big enough. As far as possible, three measurements were taken: anteroposterior, lateral, and the height above the top of the head. A rough estimate of the volume of the tumour could be made from these measurements. In each litter at least one of the tumours was allowed to grow untreated as a control, another was used for further grafting, while the rest were subjected to x-radiation as soon as possible after the lump was first noticed.

A certain number of the animals died unexpectedly and the tumours and brains of these were fixed in formalin. The rest were killed when it was expected that they could not survive until the next day. The brains of these were fixed in Zenker's solution. Serial paraffin sections were cut at 10 μ and were stained in haematoxylin and eosin, by Feulgen's method, by a modification of the azan method, and by Mallory's phosphotungstic acid haematoxylin. Some specimens were stained by Wilder's method for reticulin fibres and by Alzheimer and Mann's method for glial fibres.

Results Thirty-five mice from the laboratory stock and 42 of the N₁ strain, making 77 animals in all, were used for implantations of methylcholanthrene powder. In the laboratory stock 13 sarcomata and 6 gliomata developed. Among the 24 sarcomata there were 4 rhabdomyosarcomata. These were apparently due to some of the methylcholanthrene working back through the skull before healing of the bone had taken place.

There were some quite definite macroscopic differences between the induced sarcomata and gliomata which, with some



Fig 1 Mouse with transplanted tumour

experience, made it possible to be fairly sure to which group a given tumour belonged even before it had been examined histologically. All the sarcomata, including the rhabdomyosarcomata, penetrated the skull at the site of the operation and produced a definite lump on the top of the head, as well as some destruction of the brain. The gliomata remained within the skull, producing at most a generalised swelling of the head. A sarcoma was usually enclosed within a fibrous capsule, a glioma spread throughout the brain so that it was impossible to tell macroscopically where the tumour tissue ended and healthy brain tissue began. A characteristic feature of all the gliomata, whether induced or grafted, was the presence of numerous haemorrhages within the tumour.

Since an induced glioma produced no very obvious external signs, it was often extremely difficult to recognise its presence while the animal was alive. Usually an apparently healthy animal was found dead

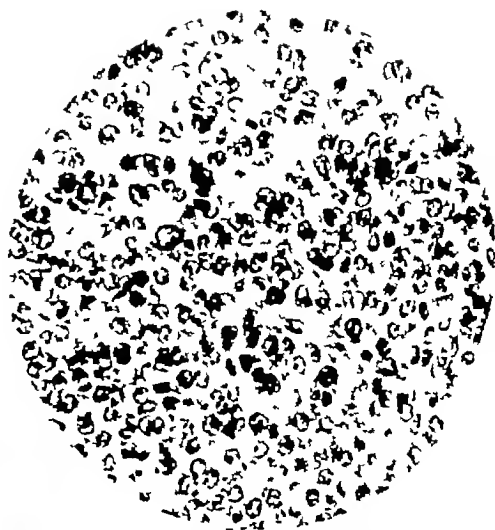


Fig 2 Section through a transplanted glioma (mouse 100c). Some normal brain tissue can be seen at the top of the photograph. Note mitoses in the tumour. Zenker, haematoxylin and eosin. $\times 410$

in its cage, and an examination of its brain revealed the presence of the tumour, too late to make grafting possible. As soon as this difficulty was realised, all the remaining animals were killed, about a year after the implantation of the methylcholanthrene. Unfortunately, only one of these 14 animals was found to be bearing a tumour, but since this appeared to be a glioma, it was grafted into the brains of a fresh litter of N₁ mice and is the parent of all the grafted tumours with which the present investigation is concerned.

Each type of tumour obtained, fibrosarcoma, rhabdomyosarcoma, and glioma, bred true to graft. Several passages (a maximum of 7 in the case of the glioma) made no difference in the histological appearance of the tumour tissue. Since this paper is mainly concerned with the maintenance and reactions of gliomata, the histology of the sarcomata will not be considered here.

Grafts of glioma tissue were successful in every animal that survived the operation (85). The average interval elapsing between the operation and the first appearance of a lump or swelling was twenty-three days, the longest period sixty-five



Fig. 3 Section through a transplanted glioma (mouse 99A), stained by Wilder's method for reticulin. Note the absence of fibres except around the capillary. Compare with Figs 4 and 5. Zenker-Wilder $\times 825$.

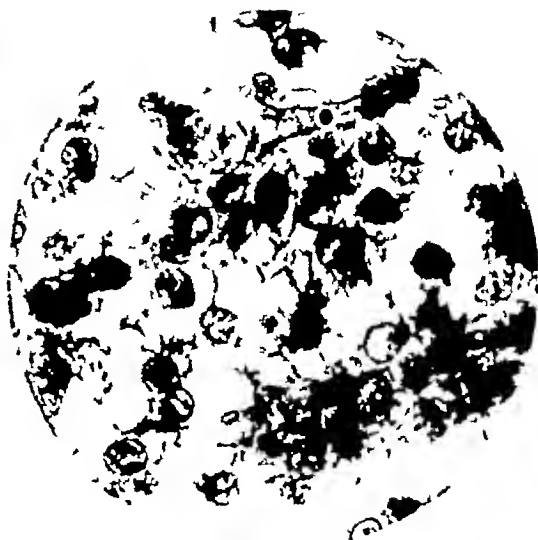


Fig. 4 Another part of the tumour shown in Fig. 3 (mouse 99A), stained by Alzheimer and Mann's method for glial fibres. Note the network of fibres connecting the tumour cells. Compare with Figs 3 and 5. Zenker, Alzheimer and Mann $\times 825$.

and the shortest ten days. The average time for an induced glioma was 29.3 days, the longest and shortest periods being 39.7 and 17.0 days, respectively.

The grafted gliomata, probably because they grew so quickly, differed from those that were induced in that they usually broke through the skull at the site of the operation, producing an easily recognisable lump on the head (Fig. 1).

Figure 2 shows a section of one of the grafted gliomata. It is mainly composed of small cells with star-shaped cytoplasm and is relatively undifferentiated. In general appearance it is like the cerebral tumour described by Lopez in a rat and said by him to resemble a human glioblastoma isomorphus. A fair number of mitoses are present. Staining by Wilder's and the azan technique showed no reticulin fibres (Fig. 3) except along the vessels. On the other hand, Alzheimer and Mann's method for glial fibres revealed a fine network of blue-grey fibres connecting the tumour cells (Fig. 4). In this respect the tumour showed a marked contrast to the sarcomata, in which many reticulin and collagen fibres, all running roughly parallel to one another, were easily demonstrated (Fig. 5). These staining reactions provide convincing

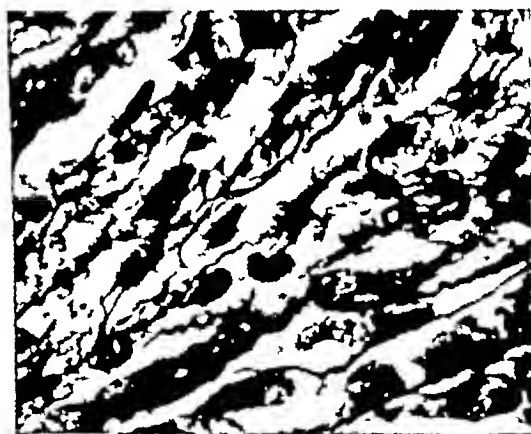


Fig. 5 Section through a transplanted sarcoma (mouse 42c) stained by Wilder's method for reticulin. Note the numerous fibres all running roughly parallel connecting the tumour cells. Compare with Figs 3 and 4. Zenker-Wilder $\times 825$.

evidence that the tumour really is a glioma.

The tumour cells can be seen invading the brain particularly through the perivascular and ventricular spaces, they also penetrate the actual brain tissue and are often grouped round the ganglion cells. There is no reaction on the part of the normal brain tissue and no round-cell infiltration.

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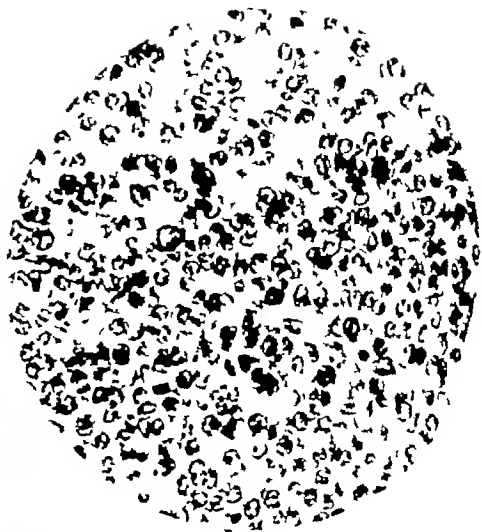


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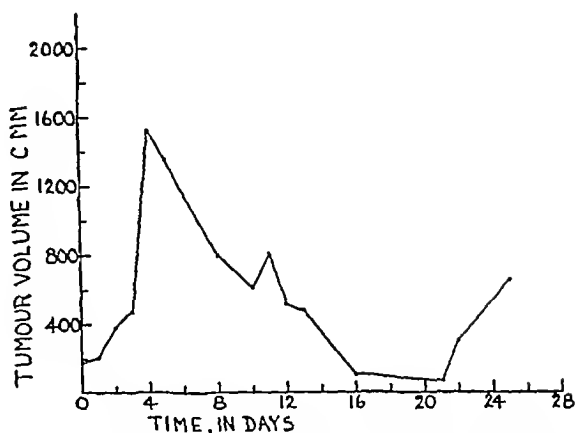
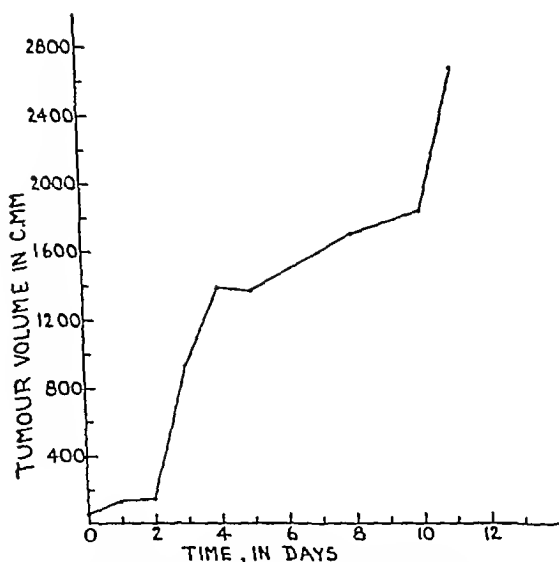


Fig 8 (left) Growth of transplanted glioma in mouse 111G. Irradiation with 3,247 r has had no very marked effect on the rate of growth. Compare with Fig 9. Abscissae: Time in days. Ordinates: Volume of tumour in cubic millimeters.

Fig 9 (right) Growth of transplanted glioma in mouse 111F. This animal was a litter mate of 111G. Both had a piece of the same tumour grafted into the brain on the same day, each first showed a measurable lump after eighteen days, each was exposed to a dose of 3,247 r four days later. Note the decrease in size of the tumour after irradiation. Abscissae: Time in days. Ordinates: Volume of tumour in cubic millimeters.

tube was adjusted and the exposure given. The animals were sometimes restless in spite of the anaesthetic, so that it was necessary to fix the limbs and body to the base of the box with adhesive tape to prevent their moving during the exposure.

The dose rate was determined with the apparatus set up as in Figure 6 but without the cover C in place, so that the beam of radiation could reach the ionization chamber of a Siemens dosage-rate meter mounted at a known distance below the centre of the box. The dose rate at the position occupied by the mice was measured by means of small condenser ionization chambers (24), the dose rate on the Siemens dosimeter was recorded at the same time. The latter thus served as a monitor for the dose delivered to the animals, and for each set of irradiations the conditions were checked and, if necessary, adjusted by means of the monitoring dosimeter. The dose delivered by this technique is not perfectly uniform throughout the part of the brain exposed, but, having regard to the average dimensions of the mouse brain, its distance from the focus and the quality of the radiation, it is not

likely that the doses received by any given part of a brain or tumour varied by more than about 10 per cent from the average values.

Results Thirty-nine of the 85 grafted tumours were irradiated, of these, 12 received a dose of 1,623 r, 10 a dose of 2,434 r, 2 a dose of 2,850 r, and 15 a dose of 3,247 r.

The effect of irradiation on the growth of the tumours was very variable. In some individuals a dose of as much as 3,247 r seemed to have no effect whatever on the rate at which the size of the tumour increased (Fig 8) while in others, sometimes litter mates, the tumour decreased in size and might even disappear altogether for a time (Fig 9). However, in no case was the tumour entirely destroyed, even in a mouse where the lump did not reappear and the postmortem examination showed no swelling, histologic examination revealed the presence of tumour tissue in the brain, although the whole of the left and much of the right hemisphere had completely disappeared, leaving a cavity full of fluid in their place.

In general, the higher doses were more effective in arresting the tumour growth.

PART II

Method In order to ensure that the mice did not move during the exposure to radiation they were lightly anaesthetised with nembutal. An intraperitoneal injection of 0.01–0.05 gr nembutal in saline (the amount varying with the weight and response of the animal) was given immediately before the exposure. The usual dose was 0.02 gr for a mouse of 15–20 gm.

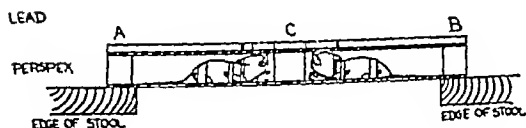


Fig 6 Complete arrangement for irradiation side view

The x-radiation used was generated at 180 kv (Villard circuit) and filtered by 0.5 mm Cu + 1.0 mm Al, the half-value layer of the radiation was 0.95 mm Cu, corresponding to an effective wave length of about 0.16 \AA . The distance from tube focus to the centre of the mouse brains was approximately 25 cm, the mean dose rate was 154 r/min in all the experiments. Up to 4 animals could be irradiated at once.

The apparatus in which the animals were exposed (Fig 6) was designed as a complete box to prevent the mice escaping into the hospital if they recovered from the anaesthetic during the irradiation. The box was mounted 70 cm above the floor

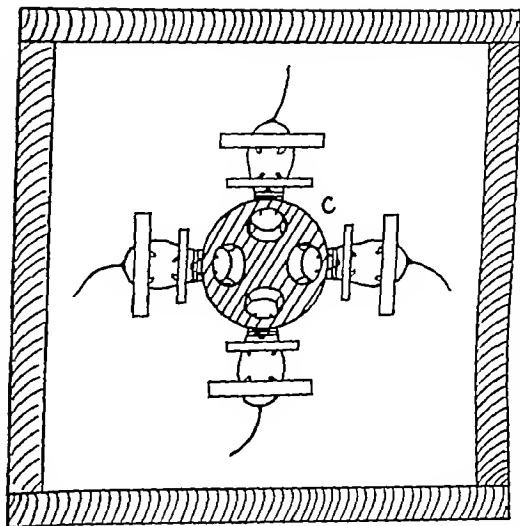


Fig 7 Arrangement of four mice underneath the windows in the lead cover C before the lid AB is placed in position

between two stools. Experiments with normal mice had shown that if the animals were to survive the irradiation by more than about ten days, it was essential to protect the upper respiratory and alimentary tracts, severe radiation reactions had also been produced by exposure of the ears and eyes. For these reasons the apparatus and method of mounting the animals inside it were designed to expose as much of the brain and as little other tissue as possible.

The upper lid of the box ACB (Fig 6) was made in two parts, a circular cover, C (Fig 7) fitting into a hole in the centre of the lid proper. The lead sheet of the cover C contained 4 elliptical windows through which the x-rays could reach the brains of the animals beneath (Fig 7).

Before the exposure, the cover C was placed over the centre of the box, where it was held in position by a wooden base. The anaesthetised mice were adjusted beneath the windows with their heads bent as far forward as possible, a strip of adhesive tape fastening the nose to the neck maintained this position (Fig 6). The remainder of the lid AB was then put in place so that, except for the windows, the animals were completely screened by a sheet of lead 6 mm thick. The x-ray

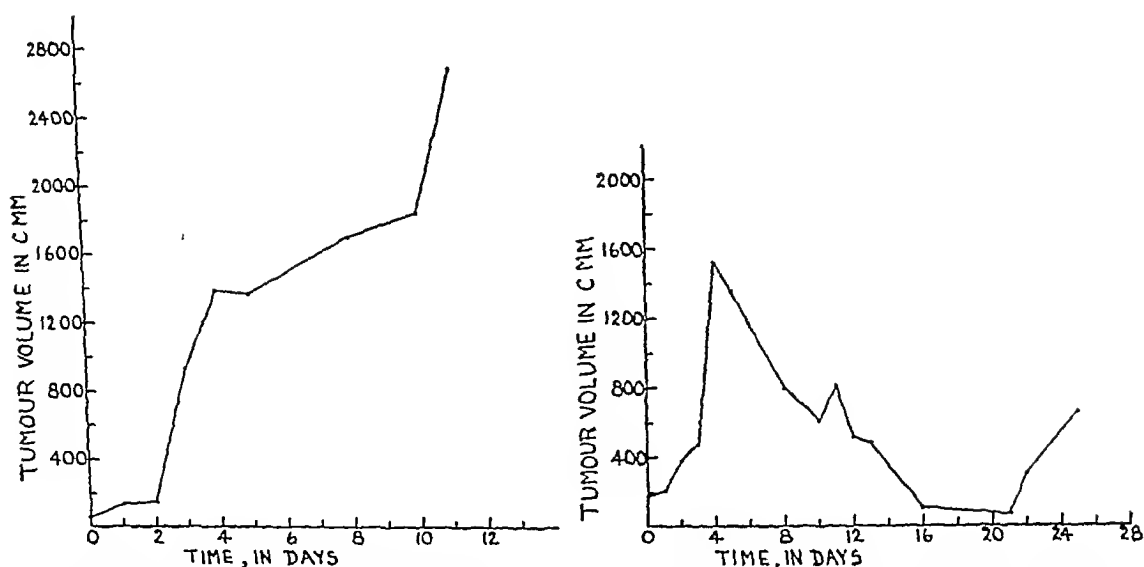


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In general, the higher doses were more effective in arresting the tumour growth

With a dose of 1,623 r the growth of 2 out of 12 tumours irradiated was temporarily arrested, with 2,434 r the figure was 5 out of 10, with 3,247 r, 6 out of 13. The survival times after the different doses are given in Table I.

TABLE I SURVIVAL PERIODS AFTER IRRADIATION

Dose (r)	No mice Irradiated	Average Time of Survival After Exposure (Days)	Shortest Survival Time (Days)	Longest Survival Time (Days)
1,623	14	8.1	0	30
2,434	9	13.8	0	21
2,850	2	9.5	6	13
3,247	9	9.7	7	18
3,247 (enlarged aperture)	5	21.6	0	54

Eight mice were killed or died within forty-eight hours of the exposure to x-rays, and histological examination showed that mitosis had entirely disappeared from the tumour tissue. Later, however, it reappeared.

Brains which were examined from seven to eighteen days after irradiation showed widespread necrosis and diffuse bleeding in the tumour tissue. Five animals which died suddenly either during or within a few hours of the exposure all had profuse haemorrhages from the tumour tissue.

Of the 23 irradiated tumours examined histologically more than seven days after the exposure, 18 had areas full of multinucleate symplasms (Fig 10). Often these areas also contained giant cells, a number of which showed abnormal mitosis (Figs 11-13). The appearance of multinucleate and giant cells was more widespread and the cells were bigger the longer the animal survived irradiation.

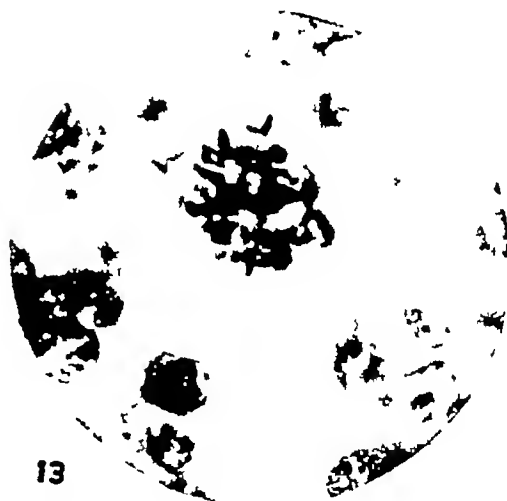
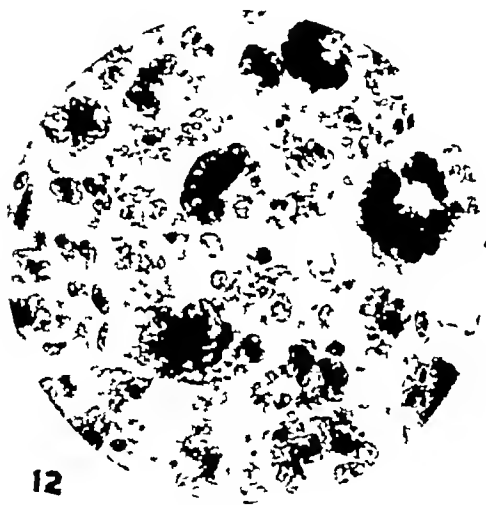
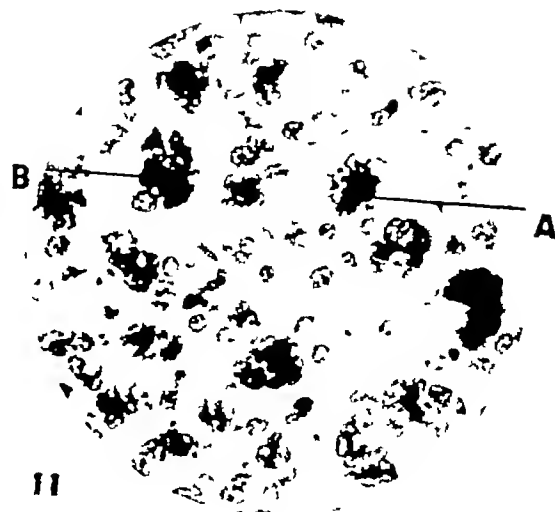
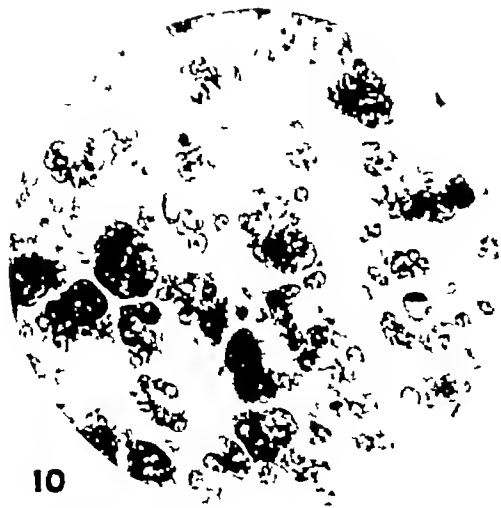
DISCUSSION

As mentioned above, several animals died suddenly and unexpectedly either during the exposure to radiation or soon afterwards. In all these cases postmortem examination revealed fresh and extensive haemorrhage from the tumour tissue. This finding emphasises the warning

sounded by several writers with clinical experience (5) of the danger of cerebral haemorrhage when certain types of human glioma are given radiotherapy.

The failure to produce any complete cures, although the growth of the tumour was arrested in a fair proportion of cases, is also in line with modern experience of human material. Peirce, Cone, Elvidge, and Tye (14) report considerable temporary benefit from x-radiation, but the symptoms recurred, with fatal results in most of their cases and, although in favour of irradiation where surgical removal is not possible, these authors do not claim to do more than add a few extra years to their patients' lives. Peirce and his fellow-workers usually use higher doses than we considered desirable for mice; they recommend 10,000-15,000 r in daily 100 r doses. It is true that with the mouse tumours the only lump which did not reappear was given a dose of 3,247 r, but the *average* result (as measured either by the survival time or by the number of animals showing regression of the lump) with 2,434 r was at least as good as with 3,247 r.

If the failure to cure the tumour is attributable to the irradiation technique, and not to the reaction of the tumour tissue, then it is due to the difficulty of reaching all parts of the mouse brain without destroying the eyes, ears, or upper respiratory and alimentary tracts, rather than to inadequate dosage. In those cases in which the tumour's first response to irradiation was a decrease in size it was a common experience to find that swelling did not recur on the site of the old lump but laterally just above and around the ears. Subsequent histologic examination revealed that active tumour tissue had spread down between the brain and skull as well as through the ventricles, but that it had disappeared around the site of implantation. This finding suggested that an increase of the area irradiated might give better results, and consequently the aperture in the lead screen was enlarged laterally in spite of the increased risk of including the ears (with the likelihood of producing aural



Figs 10-13 Sections through a transplanted glioma (mouse 117A). The animal was killed *in extremis* twelve days after irradiation with 3,247 r. The animal was killed *in extremis* twelve days after irradiation with 3,247 r. The animal was killed *in extremis* twelve days after irradiation with 3,247 r.

Fig 10 Note the multinucleate symplasms Zenker, haematoxylin and eosin $\times 375$

Fig 11 Note one giant cell in metaphase (A) and another showing the end phases of a multipolar division (B) Zenker Feulgen $\times 375$

Fig 12 Showing two giant cells in mitosis Zenker, Feulgen $\times 375$

Fig 13 Showing a dividing giant cell Zenker Feulgen $\times 1100$

abscesses) in the irradiated area. By this method we increased the average survival time after exposure to 3,247 r from 9.7 to 21.6 days.

A graft was not considered a certain success until a recognisable lump or swelling was observed, and none of the animals was irradiated earlier. However, histologic examination revealed that even at this early stage there was already consider-

able invasion of the ventricular spaces by tumour cells, and it is possible that the recurrences were due to malignant cells located in parts of the brain beyond reach of the x-ray beam, set up by spreading of tumour tissue through the ventricles. On the other hand, it must be emphasised that with 3,247 r and an enlarged aperture the growth of some of the tumours did not appear to be at all affected by x-radiation,

With a dose of 1,623 r the growth of 2 out of 12 tumours irradiated was temporarily arrested, with 2,434 r the figure was 5 out of 10, with 3,247 r, 6 out of 13. The survival times after the different doses are given in Table I

TABLE I SURVIVAL PERIODS AFTER IRRADIATION

Dose (r)	No mice irradiated	Average Time of Survival After Exposure (Days)	Shortest Survival Time (Days)	Longest Survival Time (Days)
1,623	14	8.1	0	30
2,434	9	13.8	0	21
2,850	2	9.5	6	13
3,247	9	9.7	7	18
3,247 (enlarged aperture)	5	21.6	0	54

Eight mice were killed or died within forty-eight hours of the exposure to x-rays, and histological examination showed that mitosis had entirely disappeared from the tumour tissue. Later, however, it reappeared.

Brains which were examined from seven to eighteen days after irradiation showed widespread necrosis and diffuse bleeding in the tumour tissue. Five animals which died suddenly either during or within a few hours of the exposure all had profuse haemorrhages from the tumour tissue.

Of the 23 irradiated tumours examined histologically more than seven days after the exposure, 18 had areas full of multinucleate symplasms (Fig 10). Often these areas also contained giant cells, a number of which showed abnormal mitosis (Figs 11-13). The appearance of multinucleate and giant cells was more widespread and the cells were bigger the longer the animal survived irradiation.

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Por medio del implante de polvo de metilcolantreno a una edad temprana, produjéronse en ratones tumores cerebrales, tanto sarcomas como gliomas. Los tumores fueron conservados mediante injertos de trozos de tejido en los cerebros de otros ratones jóvenes.

Varios tumores injertados de un glioma fueron tratados con los rayos X. Hubo

mucha variación individual en la reacción de los tumores injertados a la radiación; algunos aparentemente no se afectaron, en tanto que en otros se estacionó temporalmente la proliferación. No hubo curaciones. Describense las alteraciones histológicas producidas en estos tumores por la irradiación.



so that even if we could be sure of reaching every tumour cell with an adequate dose we should still expect a fair proportion of failures

The multinucleate symplasms and giant cells, the latter often showing abnormal mitosis, were never seen in the unirradiated tumours, but occurred in some parts of most of the tumours from animals which survived irradiation by more than 7 days. They seemed to be rather more common in those tumours which responded to radiation by a decrease in size. In most cases the longer the interval between irradiation and death, the bigger the groups of nuclei. They were never seen in an actively growing part of an irradiated tumour and it seems safe to assume that their presence was a result of the irradiation.

It is already known that two common effects of irradiation are increase in cell size and abnormal mitosis, often resulting in the inability to produce complete daughter cells, with the consequent production of multinucleate cells (Politzer, 15). Therefore, it seems that the most probable explanation of the multinucleate symplasms observed in these tumours is that they are the result of repeated endomitosis of the giant cells in consequence of the irradiation.

SUMMARY

1 Cerebral tumours, both sarcomata and gliomata, were produced in mice by the implantation of methylcholanthrene powder at an early age.

2 The tumours were preserved by grafting pieces of their tissue into the brains of other young mice.

3 A number of grafted tumours from a glioma were treated with x-rays.

4 There was much individual variation in the reaction of the grafted tumours to radiation, some appeared to be unaffected while the growth of others was temporarily arrested. There were no cures.

5 The histologic changes produced in this tumour as a result of irradiation are described.

ACKNOWLEDGMENTS We owe an especial debt of gratitude to Dr A Glucksmann, without whose

encouragement and help, especially in the treatment and interpretation of the histologic material, this investigation would probably never have been completed.

We also wish to thank Mr Lenney of the Strange ways Laboratory for making the photomicrographs and Mr N H Pierce of the Physics Department, Westminster Hospital, for his assistance with the irradiations.

We thank Dr F M Allichin of Westminster Hospital for so readily giving us permission to use an x-ray set in his department for the experiments, and one of us (C W W) acknowledges the financial assistance given his department by the British Empire Cancer Campaign.

The Medical School
Birmingham England

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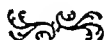
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Osteochondritis Dissecans of the Ankle

With Reports of Four Proved Cases¹

A/SURGEON COMDR C E VAUGHAN, R C N (R)² and SURGEON LIEUT J G STAPLETON, R C N (R)³

THE PATHOLOGICAL condition known as osteochondritis dissecans has a surprisingly long history in medical literature. Various writers have pointed out that Alexander Munro (18) recognized the condition in 1738. It was not until 1887, however, that König (13) gave the first accurate description of the anatomy and pathology of the condition. Both men based their reports on surgical operations and dissection of cadavers. With the widespread use of diagnostic roentgenology the diagnosis is no longer a rarity.

The name "osteochondritis dissecans" was suggested by König (14) in 1905. Although, as Burr (4) points out, it is not entirely appropriate, in that it suggests an inflammatory condition, it has become hallowed by usage and will no doubt remain along with many other terms which the march of medical progress has rendered inaccurate.

Osteochondritis dissecans is an aseptic necrosis of subchondral bone and the overlying cartilage. Usually a small area of bone adjacent to the articulating surface is affected. When it becomes necrotic, the overlying cartilage is devitalized, and frequently the entire fragment separates out and forms an intra-articular loose body. Recurrent pain, effusion, weakness, and the development of osteoarthritic changes constitute the usual sequence of events if the condition is untreated. It seems likely that the lesion properly belongs, as Phemister (20) has pointed out, in the group of aseptic necrosing lesions of bone, which includes necrosis of the fractured femoral head, Kienbock's disease, Legg-Perthes' disease, Köhler's, Freiberg's, Osgood-Schlatter's, and others.

The early writers all referred to involve-

ment of the knee joint, but many reports have since appeared describing the lesion in other areas, including the femoral head, the head of the humerus, the capitellum of the humerus, the ankle, the metacarpophalangeal joints, and recently the supra-trochlear septum of the humerus (Cryslér and Morton, 8). It appears that the condition is rather uncommon in the ankle, as few reports are to be found in the literature, and only a very occasional one in English. The earliest accounts of ankle involvement appeared in the German literature in 1927 (Breitlander, 2, Harms, 10). Subsequently, a few additional cases were published, the majority of them in foreign-language journals until, at the time of Mensor and Melody's (17) excellent review in 1941, a total of 19 cases had been recorded. Their case brought the total up to 20. Four further papers on the subject have appeared in the past five years, but unfortunately only two of these are available to us. This paper is a presentation of four additional proved cases. Three of these were seen in the Atlantic Command of the Royal Canadian Navy and one at the McGregor Clinic, Hamilton, Ontario.

The etiology of the condition has been the subject of considerable discussion, which has been well summarized by Conway (7). The main theories of origin may be divided into traumatic and non-traumatic. The latter include embolic, bacterial, and constitutional theories. The traumatic theory seems best supported by the evidence, and we feel that trauma is the major factor in these cases. It is possible, however, that some patients at least have an underlying predisposition to the condition, since it is not unusual for more than

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³ Radiologist Royal Canadian Naval Hospital Sydney N S Canada

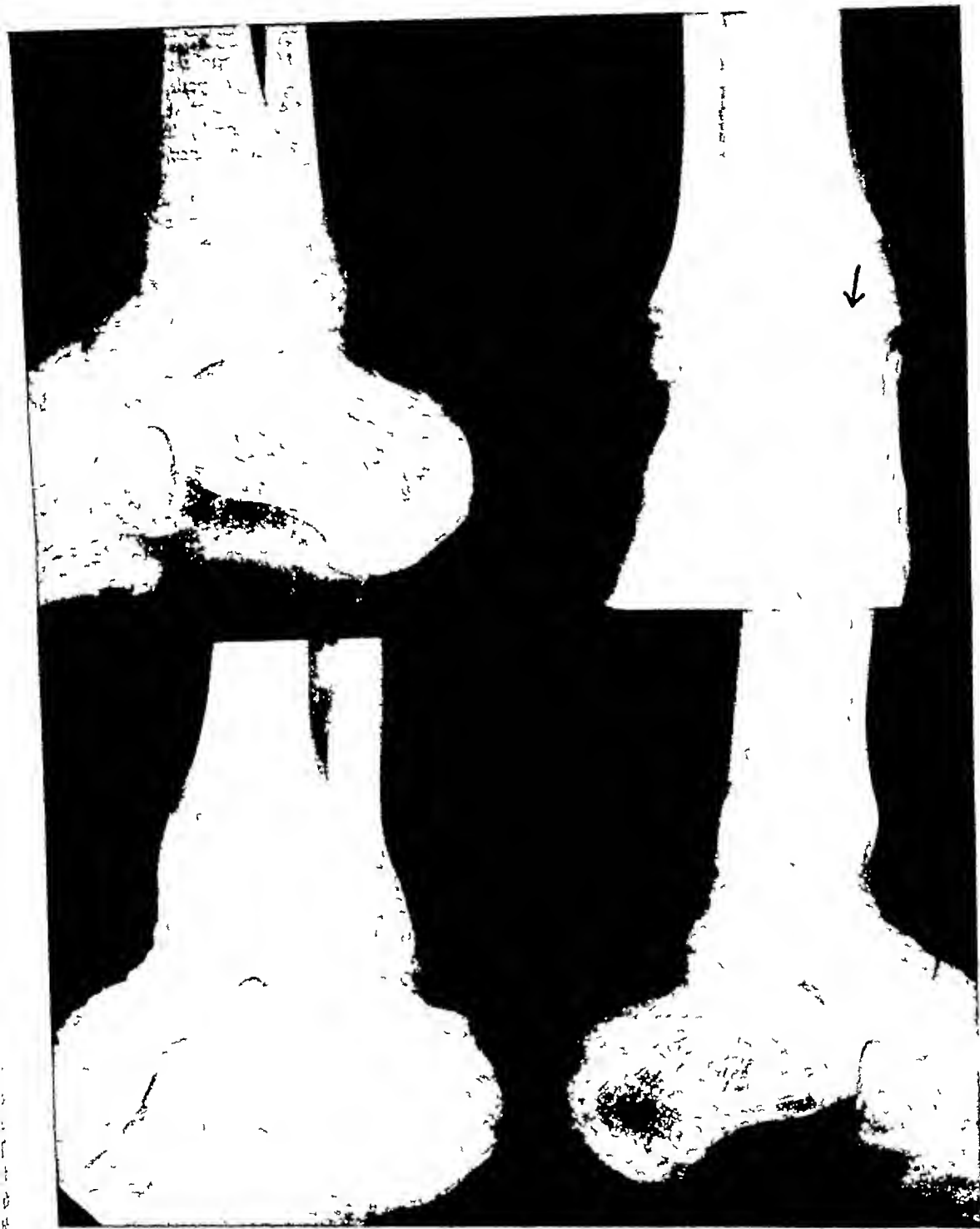


Fig 1 Case 1 Spicule of bone off medial aspect of talus Unfortunately preoperative films were un available in this case

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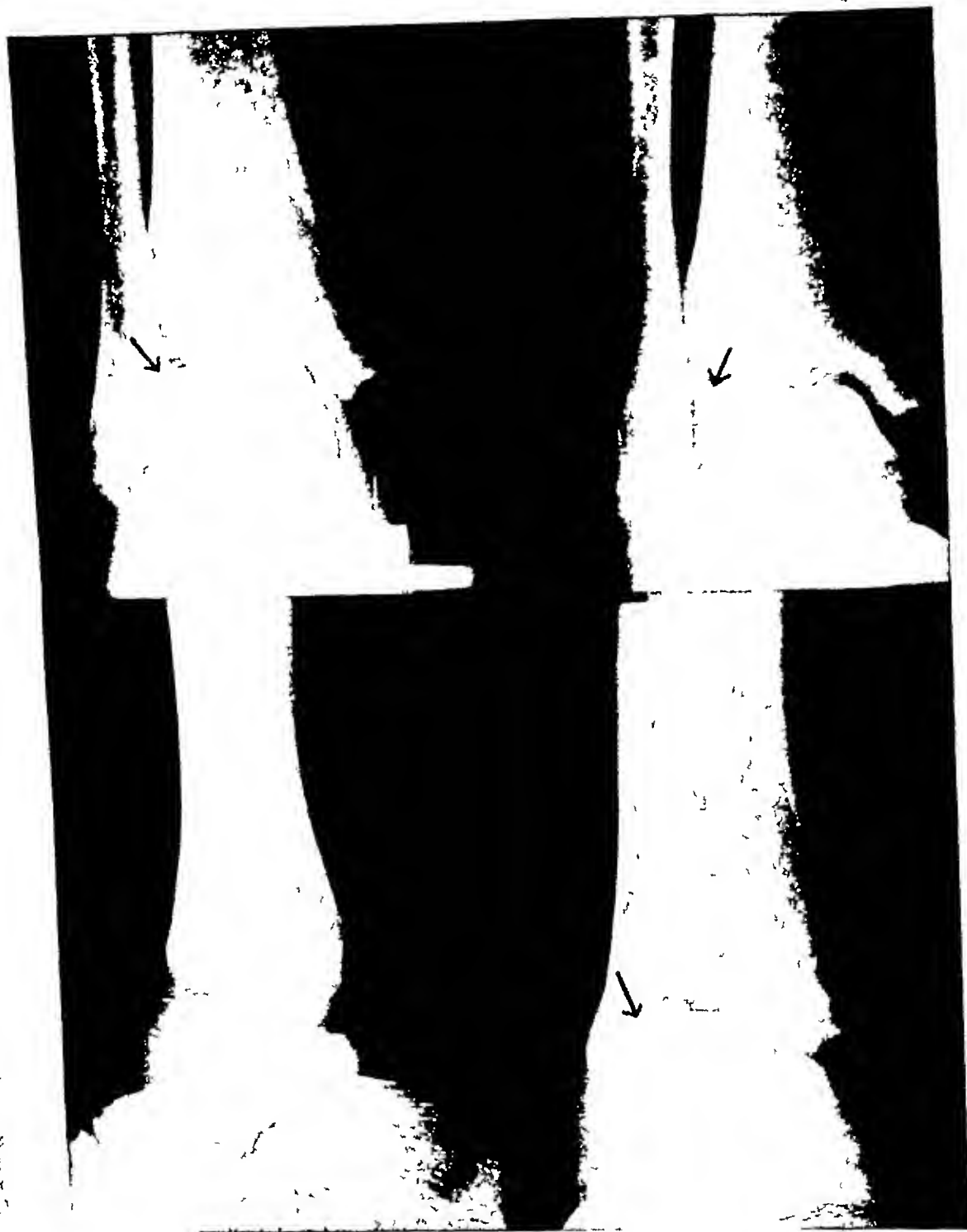


Fig 2 Case 2 Ossicle visible on superolateral surface of talus

CASE 3 (Fig 3) V F R, male, age 19, reported to sick bay on Aug 10, 1943, complaining of pain in the left ankle. He stated that for one and a half years he had had pain on the lateral side of the ankle

on walking or playing strenuous games. The joint became painful and stiff on occasions and was hard to move. It had never been actually locked. The pain had become severe a few days before. Physical

one joint to be affected, often without any definite history of injury. Perhaps there may be some metabolic or constitutional predisposing condition such as is found in many of those with slipped epiphyses in adolescence.

All writers agree that the treatment of choice is surgery, since there is no tendency for revitalization of the fragment, even in those cases where complete separation and loose-body formation have not occurred. Early surgical excision will forestall the development of the traumatic synovitis and arthritic changes which cause permanent disability.

DIAGNOSIS

Patients with ankle injuries, especially tearing of the collateral ligaments and subluxation without fracture, should be watched for the development of subsequent osteochondritis dissecans of the talus. This affects the upper portion of the articular surface, presumably due to injury by impingement against the internal surface of the malleoli during subluxation. Mensor and Melody have recommended the use of tomography as a diagnostic aid. We have not used this method. Our routine study of the ankle includes four views, and we have found that in most cases the lesion of osteochondritis dissecans is best seen in one of the oblique views. The characteristic roentgen findings are similar to those found in other joints. A small button-like fragment of devitalized bone is visualized lying in a depression at the upper margin of the trochlea of the talus on either the medial or lateral side. Usually it is demarcated from the adjacent bone by a radiolucent line. In none of our cases had the condition progressed to the formation of a completely free intra-articular loose body, but this, no doubt, does take place. One ankle was affected in each of the cases here reported, but bilateral involvement is known to occur. Both ankles were affected in a patient seen by a local orthopedic surgeon while in military service in Italy (12). Only one side was causing symptoms at the time

SUMMARIES OF CASE HISTORIES

CASE 1 (Fig 1) A C., male, age 55, reported on Aug 6, 1941, complaining of pain in the right ankle, present for six to seven years. He said that the ankle was weak and frequently "turned over," that it had been sprained several times, and that when he "went over" on his ankle he had a very sharp pain in the joint followed by a persistent ache for the rest of the day. Pain and aching were sufficient to interfere with his work. Clinical examination suggested a recurrent subluxation. Treatment was conservative for about eight weeks, but no improvement occurred. On Oct 4, 1941, an x-ray film showed a defect in the medial portion of the superior surface of the talus.

Diagnosis Osteochondritis dissecans

Operation On Oct 7, the joint was explored. "There was a circular piece of cartilage noted on the inner weight-bearing portion, which was loose and divided into two pieces. These were lifted out, and by curetting, a cavity $1\frac{1}{4} \times 1\frac{1}{4}$ inch was cleaned. A culture was taken. A cast was applied.

Pathological Examination No organisms were demonstrated by smear or culture. The pathologist reported osteochondritis dissecans.

Follow-Up Progress was good and x-ray studies showed filling in of the defect until April 1942, when the patient complained of pain over the internal side of the joint on walking, and a small spicule of bone fractured off the medial margin of the talus was demonstrated roentgenographically (Fig 1). This was removed by operation on April 7.

On May 23, 1942, x-rays showed that the bony spicule had been removed and that the original area of osteochondritis was filling in still further. The patient was followed until July 1942, when function was excellent and he returned to work. He was to be kept under observation by his plant nurse. He has not returned to the clinic.

CASE 2 (Fig 2), H B., male, age 22, reported to sick bay on June 30, 1944, stating that he had turned his ankle while attending a staff picnic on June 19. He complained of persistent swelling and pain. Physical examination showed moderate edema around tip of external malleolus and tenderness over anterior aspect of ankle joint. Radiographically a small piece of bone, approximately 1 cm in diameter and 2 mm in depth, was seen to be separated from the lateral portion of the superior surface of the talus. It was elevated about 1 mm from its bed. No other abnormality was noted.

Opinion Osteochondritis dissecans of talus

Operation On July 24, an area of partially separated cartilage $1 \text{ cm} \times 0.5 \text{ cm}$ was taken out with a curette, leaving a space appearing larger than the fragment.

Convalescence was complicated by a mild wound infection. The patient was discharged on Sept 14, 1944 walking without distress.

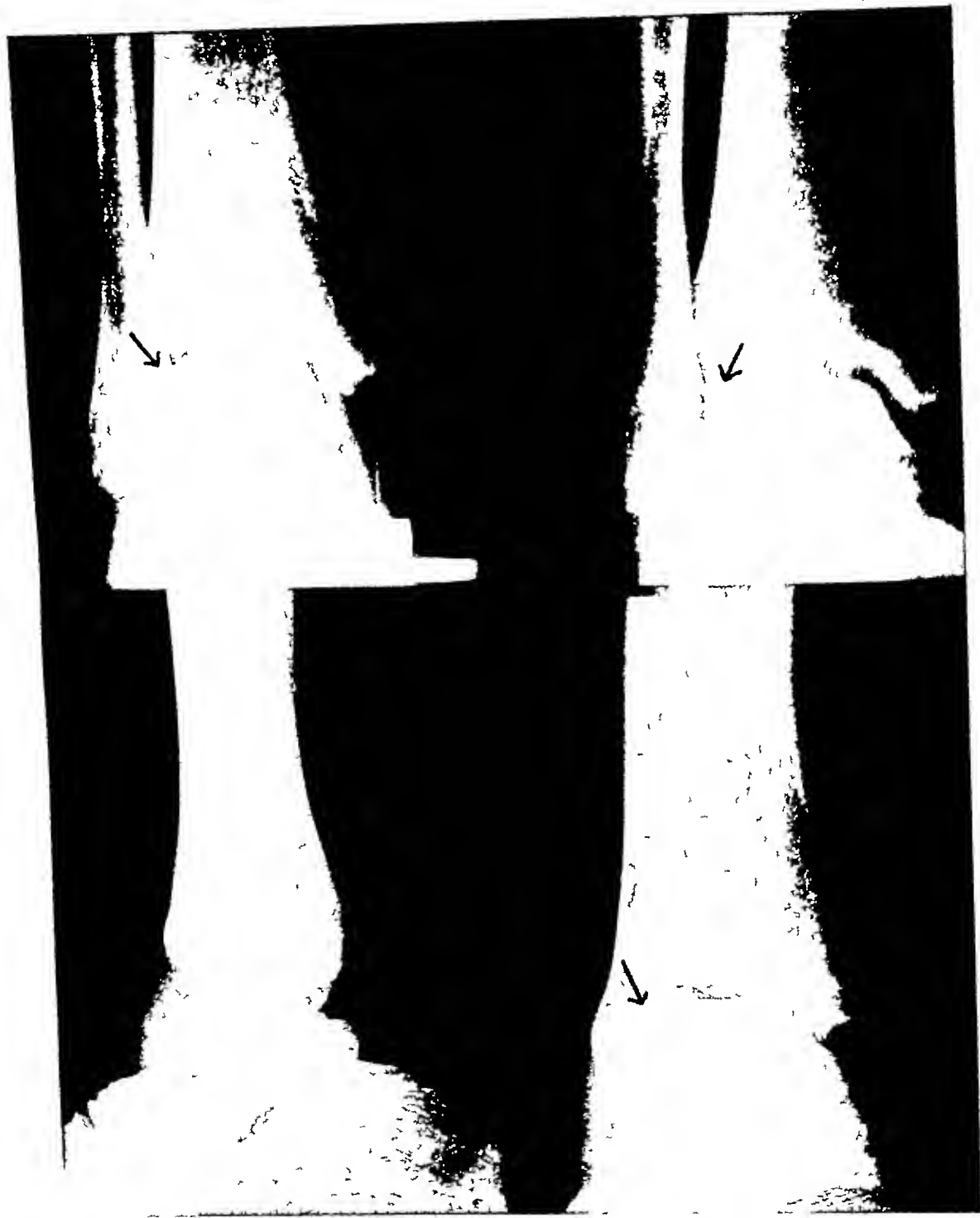


Fig 2 Case 2 Ossicle visible on superolateral surface of talus

CASE 3 (Fig 3) V F R, male, age 19, reported to sick bay on Aug 10, 1943, complaining of pain in the left ankle. He stated that for one and a half years he had had pain on the lateral side of the ankle

on walking or playing strenuous games. The joint became painful and stiff on occasions and was hard to move. It had never been actually locked. The pain had become severe a few days before. Physical

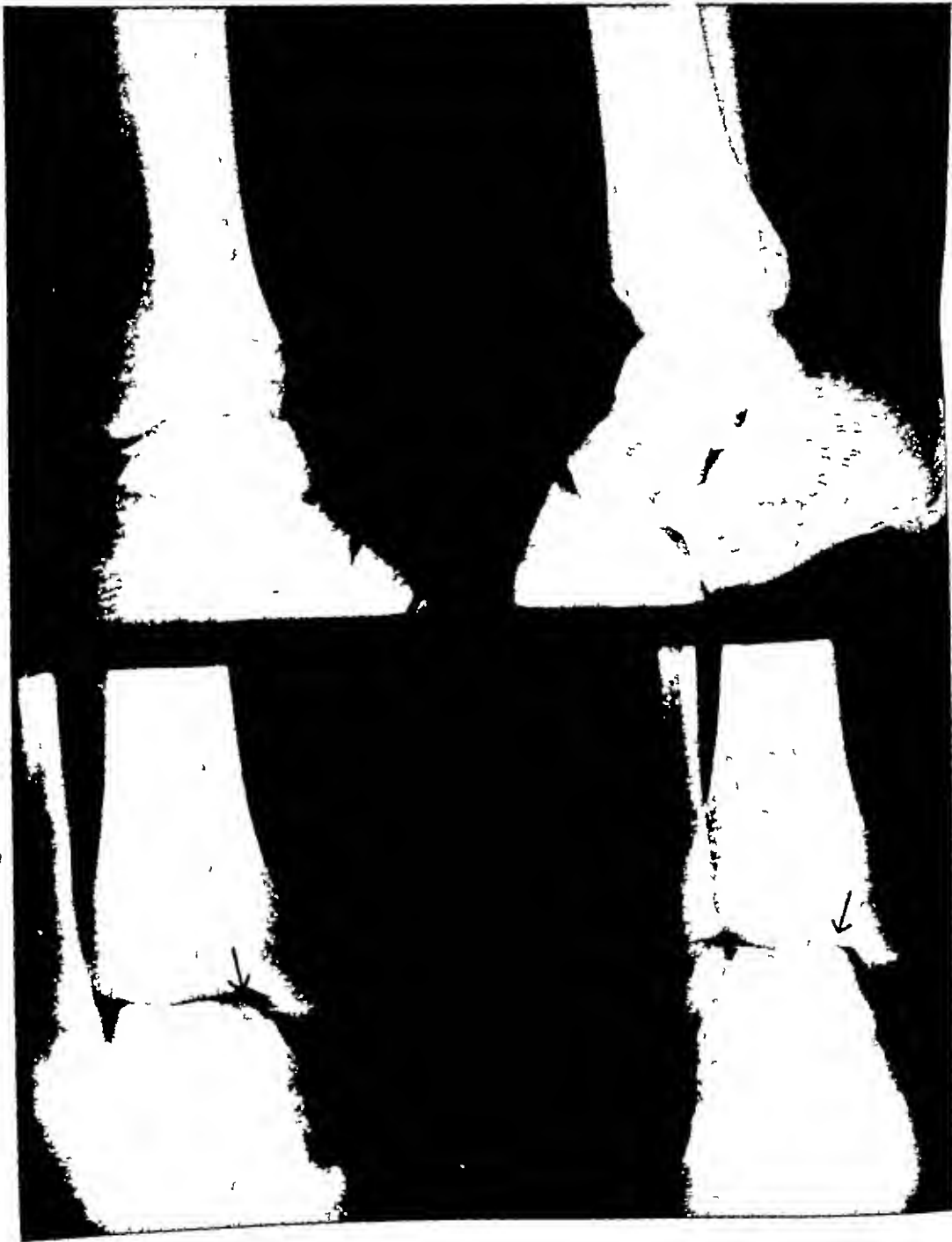


Fig 3 Case 3 Ossicle visible on upper medial surface of talus

examination showed swelling of the ankle and tenderness one inch anterior to the tip of the external malleolus
Films were made of the left ankle region in four

positions These showed an osteochondritis dissecans of the upper surface of the talus A small fragment of bone $1/4$ inch in each diameter lay on the extreme medial aspect of the upper articular sur-

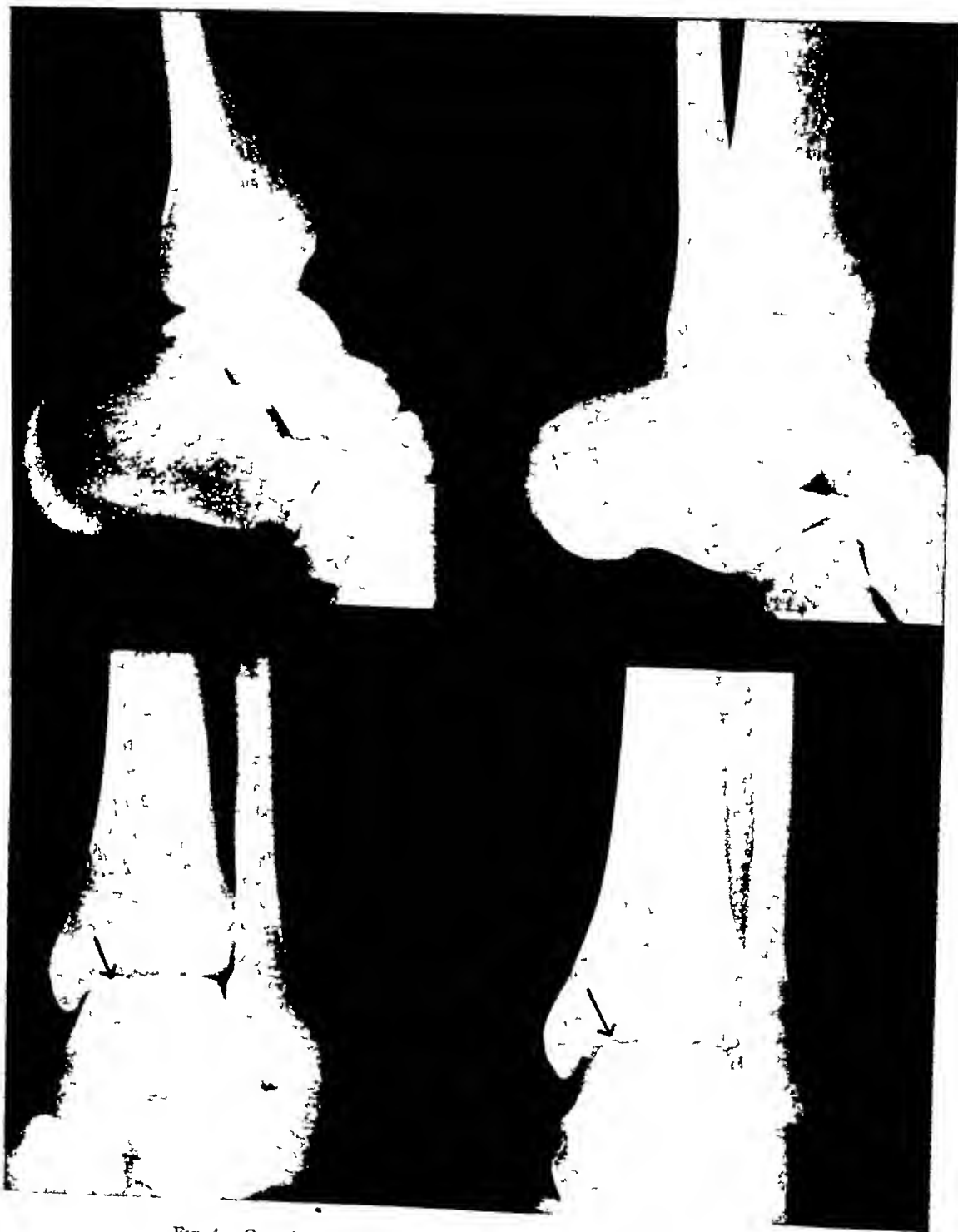


Fig 4 Case 4 Ossicle separated from superomedial aspect of talus

face of the talus. Films of the right ankle in four positions were negative.

Opinion Osteochondritis dissecans of left ankle.

Operation The report of the operation (Aug 11,

1943) was as follows: 'The fragment was moveable under intact cartilage. A piece of bone 1 cm × 0.5 cm was removed through divided cartilage, leaving a pit in the superomedial surface of the astragalus.

The base was covered with cancellous bone. Joint closed with firm dressing."

The patient was discharged to twenty-one days convalescent leave on Sept 2, 1943.

CASE 4 (Fig 4) M. C. B., female, age 26, reported to sick bay on Jan 17, 1945, complaining of instability of the left ankle. In November 1944 she had first noticed that the ankle was unstable and appeared to "collapse," so that she tended to fall forward. In September 1944, she had undergone her initial training in the W. R. C. N. S., which had involved considerable marching. A distinct snapping sound could be heard on flexion and extension. There was slight tenderness on palpation over the anteromedial aspect of the joint. Continued pressure there prevented snapping. Crepitus was noted on flexion.

Roentgen examination showed a small fragment of bone separated from the superior articular surface of the talus on the medial side, and a diagnosis of osteochondritis dissecans was made.

Operation. At operation an "area of diseased cartilage at the extreme posteromedial aspect of the weight bearing portion of the talus, 4 mm. X 2 mm. in size, was lifted off, and the underlying soft bone curetted, leaving a saucerized depression."

The patient was discharged to convalescent leave on Feb 12, 1945, at which time she had been walking for several days without pain or discomfort. There was slight limitation of plantar and dorsal flexion.

SUMMARY

1 Osteochondritis dissecans occurs in the ankle but is not common in that situation, only 20 cases being reported in the literature up to 1941. The complete text of several subsequent reports is not available to the authors at present.

2 Four proved cases of osteochondritis dissecans of the talus are here presented. The upper medial portion of the articular surface was involved in 3 cases, and the upper lateral margin in 1.

3 With one exception, the patients were males. The ages ranged from 19 to 55, the mean age being 30 years.

4 The duration of symptoms was from one week to approximately six or seven years. There was a suggestive history of antecedent trauma in 3 cases.

5 The radiologic findings were very similar to those in osteochondritis dissecans of the knee. A small button-shaped fragment of bone was observed subjacent to the articular cartilage on the superior

surface of the talus. This was surrounded by a narrow radiolucent zone. The bony fragment was not lying free in the joint in any instance. Oblique views of the ankle were useful in demonstrating the lesions.

6 Treatment consisted of operative removal of the fragment and curettage of the necrotic bone.

793 Main Street East
Hamilton Ontario
Canada

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SUMARIO

Osteocondritis Disecante del Tobillo, con Historias de Cuatro Casos Comprobados

La osteocondritis disecante se presenta en el tobillo, pero no es frecuente en dicho sitio, pues la literatura no revela más que 20 casos hasta 1941. En este trabajo describen cuatro casos comprobados en 3 estaba afectada la porción meso-superior de la cara articular y en 1 el borde latero-superior. La edad de los enfermos varió de 19 a 55 años, promediando 30. Tres de los enfermos eran varones. Los síntomas habían durado de una semana a unos 6 ó 7 años. En 3 casos había antecedentes indicativos de traumatismo.

Los hallazgos radiológicos fueron muy semejantes a los de la osteocondritis disecante de la rodilla. Subyacente al cartílago articular de la cara anterior del astrágalo observóse un fragmentillo óseo en forma de botón, rodeado de una estrecha zona radiolúcida. En ninguno de los casos se hallaba libre en la articulación el fragmentillo óseo. Las vistas oblicuas del tobillo resultaron útiles para descubrir las lesiones.

El tratamiento consistió en la extirpación quirúrgica del fragmento y el raspado del hueso necrosado.



The base was covered with cancellous bone. Joint closed with firm dressing."

The patient was discharged to twenty-one days convalescent leave on Sept 2, 1943

CASE 4 (Fig 4) M C B, female, age 26, reported to sick bay on Jan 17, 1945, complaining of instability of the left ankle. In November 1944 she had first noticed that the ankle was unstable and appeared to "collapse," so that she tended to fall forward. In September 1944, she had undergone her initial training in the W R C N S, which had involved considerable marching. A distinct snapping sound could be heard on flexion and extension. There was slight tenderness on palpation over the anteromedial aspect of the joint. Continued pressure there prevented snapping. Crepitus was noted on flexion.

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Roentgen examination of the abdomen may confirm the suspected diagnosis of intestinal perforation. As early as 1924 Massie (5) cited a case of rupture of the jejunum in which, by x-ray studies, a localized pneumoperitoneum was demonstrated to the left of the second lumbar vertebra. He pointed out that in injuries of the lower abdomen, the pneumoperitoneum may remain localized, that the gas may pass upward only as far as the attachments of the transverse mesocolon. Christopher (2) in 1934 reported a case of intestinal rupture with the patient in good general condition and free from pain, roentgen examination in the erect position revealed free air beneath the diaphragm. Veal and Barnes (9) state that a careful x-ray study should be made in all suspected cases. In three of their six cases in which a film of the abdomen was obtained, the diagnosis of intestinal rupture was confirmed by finding free gas in the peritoneal cavity.

Even with prompt operation, the mortality rate is high. In the series of 1,476 cases collected from the literature by Poer and Woliver (7), 1,014 were submitted to operation, with 603 deaths, an operative mortality of 59.5 per cent. Wilensky and Kaufman (10) state that the mortality rate is 40 per cent for patients operated on within twelve hours, 71 per cent between twelve and twenty-four hours, and 84 per cent after twenty-five hours. Among the 462 non-operated cases in the series of Poer and Woliver there were no survivors. With the exception of the two cases cited by Veal and Barnes (9), in which recovery followed drainage of walled-off abscesses, we have found no record in the literature of survival when operation had been delayed beyond a number of hours.

In view of the experience of other observers, we consider it noteworthy that we, as radiologists, should have encountered, within a few months of each other, two cases of subcutaneous rupture of the small intestine complicating pelvic injury, with survival for months after the injury. In neither case had the diagnosis been sus-



Fig 1 Case 1 two months after injury. Disturbance of barium pattern in small intestine due to establishment of false passage between torn ends of ruptured ileum indicated by arrows. Roentgenogram (Oct 16 1944) shows mild distention of small intestine at five hours. False passage well visualized. Fractured transverse processes are also shown. Symphysis has been restored to normal width. See also Figs 2 and 3.

pected. In each instance roentgen studies revealed certain abnormalities of the small intestine not interpreted as due to rupture but of sufficient importance to warrant the operation which established the diagnosis and at which the results of injury were remedied, with resultant restoration to normal function.

CASE REPORTS

CASE 1 On Aug 17, 1944, a white male, aged 41, employed as a railroad brakeman, was accidentally pinned between the couplings of two box cars. He was admitted to the Episcopal Hospital, Philadelphia, in great pain, with a clinical diagnosis of fracture of the pelvis. There was no evidence of rupture of the bladder, although the patient was unable to void, catheterization yielded 500 cc of clear urine. He vomited three times during the day of admission.

Roentgen examination of the pelvis at admission revealed marked widening of the symphysis pubis. The separation between the pubic bones measured 2 cm. In addition there was widening of the left

Rupture of Small Intestine Complicating Injury of Pelvis

Report of Two Cases with Recovery after Delayed Diagnosis and Operation¹

D ALAN SAMPSON, M D,² and HERBERT M STAUFFER, M D³

Philadelphia, Penna

THE TERM "subcutaneous rupture of the small intestine" designates that condition in which there is severance of the continuity of the small bowel beneath an intact abdominal wall. Very frequently this rapidly fatal injury is unattended by even the slightest contusion of the superficial tissues. Ordinarily it has followed a sudden unexpected blow to the unprotected abdominal wall, as in being thrown against the handles of a motorcycle, falling against solid objects, automobile accidents, kicks in the abdomen, or the rapid opening of a parachute (8). It has also resulted from muscular effort (1, 10). Counseller and McCormack (3) state that intestinal rupture can be caused in three ways, by crushing, tearing, or bursting. According to Tinsman and Barrow (8), the rupture is rarely multiple, is located in the upper jejunum or lower ileum, and may be due to impingement of the intestine on the vertebral column or on the promontory of the sacrum.

In the presence of other severe injury, the possibility of intestinal rupture may be overlooked. While in many cases of non-penetrating trauma, an immediate diagnosis of intestinal rupture can be made because of signs of rapidly developing peritonitis, and possibly by roentgen demonstration of free air in the peritoneal cavity, one must always bear in mind that in other cases a delusive calm may mark the picture. Metheny (6) points out that, although the manifestations of peritonitis will develop rapidly if there be immediate and gross contamination of the peritoneal cavity, on the other hand, should there be very little contents in the gastro-intestinal tract, signs of peritoneal irritation

will not develop until such contamination occurs. Thus gross soiling and board-like rigidity may not be present until twelve to twenty-four hours after rupture, early diagnosis depends on the importance attached to the progress of lesser signs developing during this interval.

The ease with which an early diagnosis may be obscured, and operation delayed, has also been stressed by Veal and Barnes (9), who warn that only when the peritonitis is generalized will there be a silent abdomen, that in ruptures of the lower ileum, the intestinal contents may gravitate to the pelvis with the production of only a localized peritonitis, peristalsis being heard elsewhere. The failure to appreciate this possibility may lead to a mistaken sense of security. Thus in one of their cases (as in numerous others recorded in the literature) a fatal result ensued, while in two others the diagnosis was not made until a walled-off abscess had formed, with recovery after drainage.

The clinical manifestations of non-penetrating subcutaneous rupture are well described by Counseller and McCormack (3), Veal and Barnes (9) and Hunt and Bowden (4), to whose papers the reader is referred. Vomiting after recovery from shock is a valuable early symptom, rigidity is the most valuable single sign. Various criteria for diagnosis are described. According to Poer and Woliver (7) and Tinsman and Barrow (8), intelligent suspicion may depend on nothing more than a definite rise in the pulse rate or the absence of peristaltic sounds. Wilensky and Kaufman (10) contend that early exploration rather than watchful waiting should be the rule.

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² Radiologist, Episcopal Hospital, Philadelphia, Penna.
University of Pennsylvania.

Associate in Radiology, Graduate School of Medicine.

³ Now Assistant Professor of Radiology, University of Minnesota School of Medicine.

satisfactory functioning of the small intestine with no residual obstruction

Comment In this case the severity of the pelvic injury caused the possibility of injury to the small intestine to be overlooked. The clinicians caring for this patient stated that following admission, and for many days thereafter, shock was so great that, even had the diagnosis been suspected, operation would have resulted in death. The fact that the patient survived may seem to indicate that, if operation be delayed more than a period of hours, the chances of recovery may be greater if treatment be conservative, giving the abscess an opportunity to wall-off, as occurs in the development of an appendiceal abscess.

The roentgen findings are interesting. There was obviously an obstruction of the small intestine, with a fairly extensive region of narrowing in the lower abdomen. Post-traumatic adhesions, possibly due to an intraperitoneal hemorrhage, were considered the probable cause. That adhesions were present was demonstrated at operation, but the cause was not suspected by the radiologist. In retrospect, it is possible to recognize the false passage between the torn ends of the ileum (Fig 1), a region in which there is no semblance of any mucosal pattern.

CASE 2 A member of the United States Naval Women's Reserve, 30 years of age, sustained a compound fracture of both bones of the right leg when she was struck by an automobile on Jan 30, 1944. There was considerable soft-tissue destruction, necessitating amputation two days later, which was performed at the junction of the middle and lower thirds of the right femur. Subsequent x-ray studies disclosed fractures at the right pubo iliac junction and the right pubic body, a comminuted fracture of the right ala of the sacrum (Fig 4), and fractures of the right 8th to 11th ribs, inclusive, all of these had healed at the time of roentgen examination but from the available history could be attributed to the automobile accident.

Beginning in May 1944, shortly after transfer to the U S Naval Hospital, Philadelphia, for fitting of a prosthesis, the patient began to experience recurring attacks of pain in the right lower quadrant of the abdomen, accompanied by pain on urination, each attack lasting about a week. During these episodes there were tenderness and a varying degree



Fig 4 Case 2 Roentgenogram of pelvis eleven months after injury. Healed pubic fractures on right.

of increased resistance to palpation of the right lower abdomen. Slight temperature elevation without leukocytosis was observed during these attacks, which subsided under conservative treatment. Urologic study, including intravenous urography on Aug 3, 1944, failed to provide evidence of any urinary tract disturbance to account for the abdominal pain.

Because of pain in the amputation stump and phantom limb pain, a plastic repair of the stump and neuroplasty of the right sciatic nerve were performed on Nov 17, 1944.

The right lower quadrant pain and tenderness continued to recur intermittently, and on Jan 29, 1945, a barium enema examination revealed persistent abnormal indentations in the most proximal segment of the large bowel which could be filled, presumably the cecum, it was found impossible to fill the terminal ileum during this study. Oral administration of barium resulted in demonstration of an attenuated segment of terminal ileum several centimeters in length immediately proximal to the ileocecal junction. Marked distortion of the cecum was observed (Fig 5). In view of the local tenderness and the appearance of the bowel, a roentgen diagnosis of inflammatory ileocecal mass was offered.

The abdomen was opened Feb 20, 1945, more than a year after injury. The transverse colon and a loop of ileum 12 inches from the ileocecal valve were found bound in a mass involving these two struc-



Fig 2 Case 1 Spot film (Oct 23 1944) seventy minutes after ingestion of barium

sacroiliac joint but none of the right. No fracture was detected anywhere in the pelvis. There was, however, a fracture of the left transverse process of the fourth lumbar vertebra, the only vertebra shown by this examination.

On Aug 19 the patient was placed in a Weil sling. Vomiting occurred numerous times during the first few days after admission. On Aug 18 the abdomen, which had previously been only slightly distended, although with marked tenderness in the left lower quadrant, was found to be board like and exquisitely tender over all four quadrants. His coughs were troublesome, and peritonitis was suspected. However, retroperitoneal hemorrhage was considered the probable cause of these manifestations. Subsequently the patient's general condition improved, although bouts of vomiting occurred at intervals.

During the first ten days after entry the temperature ranged up to 103° , usually about 100° , the pulse ranged between 72 and 100, the respirations averaged 24. Subsequently the temperature did not exceed 99.4° except on a few occasions. The white blood count on ten determinations from Aug 17 through Sept 28 varied between 11,900 and 23,100, averaging 17,400.

On Oct 12 the patient was removed from the sling and the pelvis was re-examined roentgenographically. The symphysis pubis was found to be practically normal in width, with the right pubic bone only about 3 mm higher than the left. The left sacroiliac joint was also practically normal in width. Because of the vomiting and persistence of abdominal pain, roentgen studies of the gastro-intestinal

tract were carried out at this time (Oct. 16 and Oct. 23). The stomach was found to be normal, with no disturbance of motility, at two hours it contained only a trace of barium. However, by exposure of serial films for visualization of the small intestine, an obstruction was demonstrated in the lower abdomen near the mid-line. Spot films exposed at seventy minutes following ingestion of the barium showed a region of narrowing of the small intestine in the lower central abdomen. The jejunum proximal to this obstruction was grossly dilated. Al-



Fig 3 Case 1 Distention of intestine well shown at four and a half hours (Oct 23 1944)

though the head of the barium column entered the cecum at five hours, there remained localized collections of barium in the small intestine in the lower abdomen, and even at twenty four hours there was still a small quantity of barium present. The examination was interpreted as demonstrating the presence of adhesions (Figs 1-3).

Laparotomy was performed Oct 26. It revealed complete transverse laceration of the terminal ileum, which had been walled off by inflammatory tissue consisting of omentum and part of the sigmoid colon which had been drawn over. These adhesions were broken up and the sigmoid was restored to the normal anatomic position. An end-to-end entero-enterostomy was performed.

The patient's recovery was complicated by an incisional hernia which was repaired at a secondary operation in February 1945. Roentgen studies Aug 23, 1945 (eight months after operation) showed

satisfactory functioning of the small intestine with no residual obstruction

Comment In this case the severity of the pelvic injury caused the possibility of injury to the small intestine to be overlooked. The clinicians caring for this patient stated that following admission, and for many days thereafter, shock was so great that, even had the diagnosis been suspected, operation would have resulted in death. The fact that the patient survived may seem to indicate that, if operation be delayed more than a period of hours, the chances of recovery may be greater if treatment be conservative, giving the abscess an opportunity to wall-off, as occurs in the development of an appendiceal abscess.

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The abdomen was opened Feb 20, 1945, more than a year after injury. The transverse colon and a loop of ileum 12 inches from the ileocecal valve were found bound in a mass involving these two struc-



Fig 5 Case 2 Narrowing of terminal ileum shown following oral administration of barium

tures and the cecum, and adherent to the posterior portion of the iliac bone at the site of an area of inflammation in the region of the ileocecal valve. A perforation of the ileum near the ileocecal valve was found within this inflammatory mass. The abnormal intestinal opening was closed and an ileocolostomy was performed.

Convalescence was slow. On April 28, 1945, an abscess, containing 6 to 8 ounces of purulent material, situated between the cecum and surface of the ilium, was drained, and subsequently a fecal fistula developed. On Aug 3 the abdomen was re-entered. The cecum and terminal ileum were dissected from the fistulous tract to the exterior. It appeared as if the opening in the ileocecal region previously closed by suture had reopened and formed the fistula. The ileocolostomy was functioning in excellent fashion and the terminal ileum was therefore divided from the cecum and the end of each closed.

The subsequent course has been uneventful, the fistula healing by granulation and bowel function returning to normal. At the time of writing (October 1945), the patient is ambulatory, using an artificial limb successfully.

Comment This case closely resembles Case 1. Pelvic and other injuries caused the possibility of intestinal injury to be overlooked. In view of the lapse of five months between the time of injury and the onset of gastro-intestinal symptoms, it is

probable that the intestinal rupture was small and that the slow escape of intestinal contents from it favored the formation of a localized abscess, overlooked because shock was attributed to skeletal damage.

The roentgen studies, as in Case 1, were correctly interpreted as indicating the presence of inflammatory changes with resultant constriction of the ileum and interference with the passage of contents through it.

SUMMARY

Two cases of subcutaneous non-penetrating rupture of the small intestine are reported. These cases are remarkable in that survival occurred in spite of delay in diagnosis and operation, in one case of more than two months, in the other case of nearly thirteen months, whereas the mortality rate in such delayed cases has previously been considered 100 per cent. In one case roentgen studies demonstrated the existence of a fistulous tract between the torn ends of the small intestine. In both cases they showed considerable localized obstruction due to post-traumatic inflammatory changes. No other such cases, with roentgen studies, have been found in a search of the literature.

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Philadelphia 25 Penna

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Rotura del Intestino Delgado como Complicación de Lesión de la Pelvis Reposición a pesar de la Tardanza en el Diagnóstico y la Intervención Comunicación de Dos Casos

Comunicanse dos casos de rotura subcutánea no penetrante del intestino delgado Estos casos son notables por haber sobrevivido los enfermos a pesar de la tardanza en el diagnóstico y la operación, que en un caso se demoraron más de dos meses, y en el otro casi trece meses, aunque la mortalidad en esos casos tardíos se había fijado previamente en 100 por ciento

En un caso los estudios radiológicos habían revelado la existencia de una fístula entre los extremos desgarrados del intestino delgado, y en ambos considerable obstrucción local debida a alteraciones inflamatorias post-traumáticas Una pesquisa de la literatura no ha revelado casos semejantes en que se hicieran estudios roentgenológicos

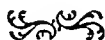




Fig 5 Case 2 Narrowing of terminal ileum shown following oral administration of barium

tures and the cecum, and adherent to the posterior portion of the iliac bone at the site of an area of inflammation in the region of the ileocecal valve. A perforation of the ileum near the ileocecal valve was found within this inflammatory mass. The abnormal intestinal opening was closed and an ileocolostomy was performed.

Convalescence was slow. On April 28, 1945, an abscess containing 6 to 8 ounces of purulent material, situated between the cecum and surface of the ilium, was drained, and subsequently a fecal fistula developed. On Aug 3 the abdomen was re-entered. The cecum and terminal ileum were dissected from the fistulous tract to the exterior. It appeared as if the opening in the ileocecal region previously closed by suture had reopened and formed the fistula. The ileocolostomy was functioning in excellent fashion and the terminal ileum was therefore divided from the cecum and the end of each closed.

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Adrenal Tumor of the Liver in a Child

Case Report with Roentgenologic Features¹

HERMAN SELTZ, M D

Elkins, W Va

ADRENAL rests have been described throughout the upper part of the abdomen in the vicinity of the adrenals Morgagni (7), in 1740, was the first to describe such accessory adrenal tissue, and Chiari (3), in 1884, was the first to report its malignant transformation Ewing (5) referred to Schmorl as recording the occurrence of adrenal rests in the liver and also tumors possibly arising from these rests, grossly resembling adrenal tumors MacMillan and Gilbert (8) reported an aberrant tumor of the upper abdomen in a fifty-one-year-old woman, with a six-year cure Griffith and Mitchell (6), in their text on *Diseases of Infants and Children*, stated that they had seen a case of adrenal tumor of the liver Nelson (9) published a series of 19 cases of accessory adrenal cortical tissue, of which 15 were in adults, but in none was the ectopic tissue located in the liver

The following case is reported because of the unusual location, in the liver, of a large ectopic adrenal tumor and the associated roentgen findings which aided in its localization

CASE REPORT

H F, a 9 year old boy was admitted to the Davis Memorial Hospital on Dec 26, 1945, for observation because of a 'lump in the stomach,' which his aunt had noticed six weeks earlier while giving him a bath The patient was a normally active child with no complaints His appetite was fair He had no nausea, vomiting, hematemesis, or abdominal pain His stools appeared normal He had no symptoms referable to the genito urinary system There had been no weight loss The mother stated that the child had jaundice at the age of three months, but this had cleared spontaneously within a few weeks

Temperature, pulse, and respiratory rate were normal The child did not appear chronically ill except for a slight pallor His nutrition was good,



Fig 1 Excretion urogram showing normal urinary tract bilaterally The large liver tumor is well demonstrated (arrows) The gas-filled duodenum is displaced to the right and the transverse colon inferiorly

and he appeared to be normally developed for his age There was no lymphadenopathy The heart and lungs were normal Blood pressure was 104 systolic and 66 diastolic A large, discrete, firm, non tender mass was present in the epigastrium and left hypochondrium The mass extended inferiorly to the umbilicus, was nodular cephalad, and moved moderately with respiration It did not appear to involve the right lobe of the liver The spleen was not palpable There was no evidence of ascites The clinical impression was (1) retroperitoneal tumor, (2) pancreatic cyst, (3) cyst or tumor of the left lobe of the liver

¹ From the Department of Radiology The Golden Clinic Elkins W Va Accepted for publication in October 1946



Fig 2 A Anteroposterior projection The barium filled stomach is displaced to the left, the antral portion of the stomach and duodenal bulb superiorly, and the descending duodenum to the right by the liver tumor The marked widening of the duodenal loop suggests a pancreatic lesion

B Left lateral projection The stomach is displaced posteriorly indicating that the tumor is located anteriorly in the region of the left lobe of the liver

Laboratory Data The hemoglobin on admission was 85 per cent, the erythrocyte count 4,020,000, the leukocyte count 6,550, with 63 per cent polymorphonuclears and 34 per cent lymphocytes. Urinalysis showed no abnormality except a 1+ albumin. The sedimentation rate was elevated to 36 mm in one hour. Icterus index was 7. The plasma protein was 7.5 gm per cent. The blood sugar was 67 mg per cent and the non-protein nitrogen 41 mg per cent. Blood Hinton and Kolmer-Wassermann tests were negative.

Röntgenological Findings An anteroposterior roentgenogram of the abdomen revealed evidence of a large, hemispherical soft-tissue mass in the epigastrium and left hypochondrium with a fairly well defined inferior border which extended down to the level of L4. The mass caused displacement of the gas-containing stomach to the left and the transverse colon and small intestine inferiorly. The right lobe of the liver did not appear to be enlarged, and its inferior border appeared smooth. The spleen was of normal size. A roentgenogram of the chest was negative.

Intravenous pyelography (Fig 1) failed to reveal any abnormality of the urinary tract. The epigastric mass did not appear to be related to either kidney.

A gastro intestinal series (Fig 2, A and B) showed

no intrinsic pathological changes in the esophagus, stomach, duodenum, small intestine, or proximal colon. The body of the stomach was displaced to the left and posteriorly, the pyloric portion and duodenal bulb cephalad, the descending duodenum markedly to the right, and the jejunum and transverse colon inferiorly, by a large epigastric mass in the region of left lobe of the liver. On Dec 31, 1945, the abdomen was explored.

Operative Findings (Dr Benj I Golden) The abdomen was opened by a left rectus muscle-splitting incision. On reaching the peritoneal cavity, a large, gray, cyst-like mass, about the size of a grapefruit, was seen protruding from the inferior aspect of the left lobe of the liver. The surface of this mass was smooth and highly vascular. Satellite discrete nodules of varying size were scattered throughout the remaining portion of the left lobe, the uninvaded parenchyma was yellow in color. The right lobe of the liver appeared grossly normal. No regional nodes were detected, nor any evidence of intraperitoneal spread. Palpation of the adjacent viscera, including the kidneys and pancreas, failed to reveal any abnormality. Two of the small nodular liver masses and aspiration material from the cyst-like mass were removed for histologic study.

Postoperative diagnosis Malignant tumor of the liver

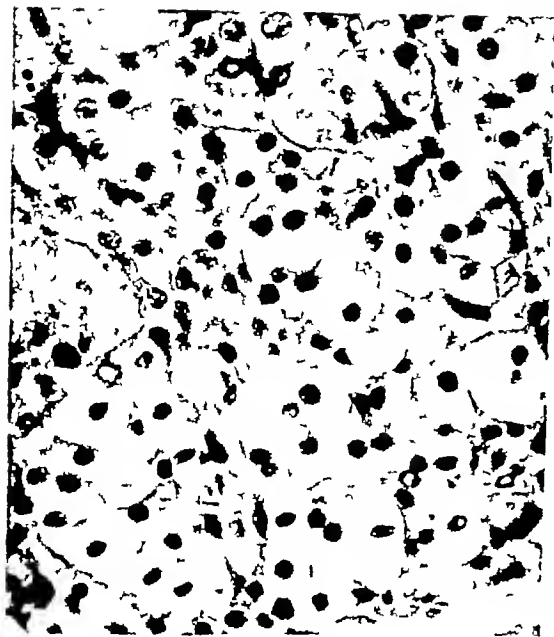


Fig 3 Section of liver mass (high power magnification) showing clear polyhedral cells resembling clear-cell carcinoma

The postoperative course was uneventful except for delayed healing of the abdominal wound. The patient was discharged from the hospital on the nineteenth postoperative day, Jan 19, 1946. Since discharge he has been seen monthly in the Out Patient Department. There has been no change in his general condition nor in the size of the tumor.

Histologic Report (Dr F Levv) Besides small areas of liver trabeculae, or structures bearing some likeness to them, the specimen showed no similarity to liver tissue. Instead of lobulae, irregular masses of more or less polyhedral cells were found (Fig 3), many of which were similar to the typical picture of clear-cell carcinoma. A continuous growth was shown by the presence of numerous mitotic figures. Large hemorrhages spread into the tumor as well as into the markedly thickened capsule of Glisson.

The description of the material from the cyst-like mass was as follows. In polarized light, unstained cells are large. Smears show double-refracting substance in the tumor cells as well as extracellularly.

The aspect of the cells, the papillary structures in some parts, the loose relation of the cells to one another in other parts, and the double refractive cholesterol esters place the growth in the group of hypernephromas. The biopsy permits no conclusion as to whether the tumor arose in or near the kidney, or is a primary growth of extrarenal misplaced adrenal rests, as these are known to occur near the solar plexus or on the inferior surface of the liver. **Pathological diagnosis** Adrenal tumor in the liver.

Comment The large mass arising from the inferior surface of the left lobe of the liver in this case produced marked widening of the duodenal loop (Fig 2, A), suggesting a lesion in the region of the head of the pancreas. The posterior displacement of the stomach (Fig 2, B), however, was inconsistent with a retroperitoneal pancreatic tumor, and for this reason the mass was considered to be in the region of the left lobe of the liver.

DISCUSSION

Roentgen studies may be of aid in the diagnosis of tumors of the liver in children, especially in localizing the tumor process, though little appears in the literature on this subject. Schatzki (12) presented a roentgenological syndrome based on the frequent association of primary hepatic carcinoma and cirrhosis which he considered highly suggestive of primary carcinoma of the liver. This syndrome consisted in the demonstration of (a) cirrhosis (esophageal varices), (b) a mass in the region of the liver, and (c) positive evidence of carcinoma (metastasis). The syndrome, however, is of little aid in children, since cirrhosis is rarely found in the young.

Hepatosplenography with the aid of intravenous thorotrast has been advocated by some (Ehrlich and Ansanelli, 4) for the diagnosis of tumors of the liver, but this procedure is rarely used by radiologists because of the possibility of late morbid changes due to the radioactivity and/or the foreign-body effect of the medium (Rigler, 11). In more recent years, the attempt has been made (Beckermann and Popken, 2; Olsson, 10) to visualize the liver and spleen with an iodized colloidal emulsion (Iodosol) as a substitute for the thorium suspension, but this, too, is not without serious danger (Olsson, 11).

Displacement and deformity of the adjacent gastro-intestinal organs by a tumor of the liver have been described by others. Abel (1) reported a case of primary carcinoma of the liver in a child, successfully treated by partial hepatectomy of the left lobe. The roentgen diagnosis in this case,

with displacement of the adjacent gastro-intestinal organs similar to our own, was pancreatic tumor

The stomach, duodenum, small bowel, and transverse colon may all be involved in the displacement process if the hepatic tumor enlarges inferiorly or posteriorly, or only the stomach itself may be displaced. If the duodenal loop is enlarged, the possibility of a tumor of the left lobe of the liver should be excluded by a lateral view. This will show anterior displacement, or no displacement, of the stomach in the presence of a pancreatic tumor or any other retroperitoneal mass in the region of the pancreas, and posterior displacement of the stomach if the mass is hepatic in origin.

If the mass in the liver enlarges cephalad, one may find a localized bulge in the diaphragm, especially on the right side. Too much emphasis cannot be placed on this finding, however, since normal developmental variations in the contour of the diaphragm occur frequently, and other intrahepatic lesions (cyst, abscess and metastatic nodules) may produce a similar diaphragmatic lobulation.

Rarely calcification may occur in a primary carcinoma of the liver. Tomlinson and Wolff (15) reported one such case in an infant with a large liver and scattered areas of calcium density in the right lobe.

SUMMARY

1 A case of aberrant adrenal tumor of the liver in a nine-year-old child is reported.

2 Roentgenologic findings which may be associated with tumor of the liver are discussed. In the case reported, displacement of the adjacent gastro-intestinal organs by the tumor caused marked widening of the duodenal loop on the anteroposterior roentgenogram, suggesting a pancreatic lesion. However the latter could be excluded by a lateral view, showing posterior displacement of the stomach.

The Golden Clinic
Elkins W Va

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SUMARIO

Suprarrenoma Hépatico en un Niño Historia Clínica con Datos Roentgenológicos

Comuníquese un caso de tumor adrenal aberrante del hígado en un niño

Repásanse los hallazgos radiológicos que pueden asociarse con los tumores hepáticos. En el caso actual, el desplazamiento de los adyacentes órganos gastro-intestinales por

el tumor provocó un ensanchamiento pronunciado del asa duodenal en la película anteroposterior, indicando lesión pancreática. Sin embargo, pudo excluirse la última con una vista lateral que reveló desplazamiento posterior del estómago.

Characteristics of X-Ray Films and Screens¹

RUSSELL H MORGAN, M D

Baltimore, Md

MOST ROENTGENOLOGISTS have long recognized the need of reliable quantitative data giving the speed, detail, and contrast characteristics of commercially available roentgenographic films and intensifying screens. From such information, the choice of the most satisfactory films and screens for use in a roentgenographic department may be greatly facilitated. Furthermore, the availability of such information to the profession would constantly stimulate the x-ray industry to improve the quality of its products.

Before quantitative data listing the characteristics of films and screens can be made generally available to the radiologist, however, four fundamental steps must be taken. First, standard definitions of speed, detail, and contrast must be established. The terms of these definitions, of course, should correspond as closely as possible to the conditions which occur when the films and screens are used in normal roentgenographic practice. Second, methods of measurement which comply with the standard definitions must be developed. Third, an impartial and able laboratory to carry out such measurements must be set in operation. Fourth, the data must be published at regular intervals in journals that have a wide circulation among radiologists.

During the past year, the laboratory of the Radiology Section, U S Public Health Service, has been engaged in investigations from which standard definitions and methods of measurement of the various film and screen characteristics may be derived. Much of this research has been completed and has been reported in previous publications (1) or publications now in prepara-

tion. It is hoped that before long quantitative data on the characteristics of all x-ray films and screens will be published regularly in the two leading radiological journals of this country.

Before these data become generally available, it may be of interest to many to observe some of the preliminary results. Measurements have been made of the detail provided by eight types of intensifying screens, one fluoroscopic screen, and several of the screen-lens-film combinations which are used in photofluorography. Data have also been derived for the contrast factors of several photofluorographic films. We are not prepared to issue any speed data on various radiographic materials at this time, since our apparatus for making these measurements has just recently been completed.

DETAIL

The ability to record detail is measured in our laboratory by determining the finest linear pattern which can be resolved by a film or film-screen combination. Most radiographic film-screen combinations are able to resolve patterns up to 10 lines per millimeter. Photofluorographic combinations, however, are generally much poorer, while films exposed to x-rays directly frequently are able to resolve patterns having 50 lines per millimeter. Indeed, the ability of films alone to record detail is so much superior to that of intensifying screens that in the case of a film-screen combination it is the intensifying screens which limit the over-all ability of the combination in this respect. As a result, it makes little difference what brand of film is used in an intensifying screen exposure as far as detail is con-

¹ From the Department of Radiology, The Johns Hopkins Hospital and the Radiology Section, Tuberculosis Control Division, U S Public Health Service. Presented at the Thirty second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec 1-6, 1946.

TABLE I RESOLVING POWER RATINGS OF COMMERCIAL INTENSIFYING SCREENS

Brand	Resolving Power (lines per mm)
Buck Xtra speed	10
Buck Mid-speed	12 1/2
Buck Detail	12 1/2
Eastman Ultra speed	9
Eastman Fine Grain	10
Eastman High Definition	12 1/2
Patterson Par speed	10
Patterson Detail	17 1/2

cerned, for any given pair of intensifying screens the detail will be the same regardless of the type of film used

The maximum number of lines per millimeter which can be resolved by a film or film-screen combination is called resolving power. Most film-screen combinations now available to the radiologist have resolving powers of approximately 10 lines per millimeter, that is, the finest linear pattern which these combinations can resolve is one having 10 lines per millimeter. In general, resolving power measurements are an excellent index of the detail provided by various radiographic materials. During our preliminary experimental work, radiographs were made with a series of film-screen combinations on which resolving power measurements were made. These radiographs were made under conditions in which loss of detail due to movement of the part under examination and to target size were reduced essentially to zero. Differences, then, in the detail exhibited by the films were the result of differences in the characteristics of the screens themselves. The radiographs were submitted to a large number of radiologists, who were asked to place the films in their order of diagnostic merit. In almost every instance the radiologists' evaluations corresponded to the quantitative resolving power measurements. Only in those instances where two film-screen combinations had almost identical resolving powers were there discrepancies, and even here the radiologist frequently stated that there was no practical difference between the two combinations.

The resolving powers of eight commer-

cially available intensifying screens are shown in Table I. It will be observed that the screens designated as high-speed by various manufacturers generally have slightly lower resolving powers than those marked mid-speed and that the mid-speed screens in turn are slightly poorer than the screens listed as high-definition. With one exception (Patterson Detail screens), however, the difference between the poorest high-speed screen and the best high-definition screen is phenomenally small. Indeed, the difference between the detail provided by screens having a resolving power of 9 lines per millimeter and those having a resolving power of 12 1/2 lines per millimeter is hardly perceptible. This fact may seem strange to many radiologists, because almost everyone can remember a time when it was not difficult to differentiate so-called high-definition screens from so-called high-speed screens from the standpoint of detail. However, with the exception of Patterson Detail screens, all of the present-day brands, regardless of designation, provide about the same detail.

The resolving power of the Patterson type "B" fluoroscopic screen is 6 lines per millimeter. This value may appear unusually high to many readers in view of the rather poor detail which can be seen under fluoroscopic conditions. This poor detail, however, is not the fault of the screen but is due to the diminished visual acuity of the observer at the low levels of illumination occurring in fluoroscopy.

TABLE II RESOLVING POWER RATINGS OF COMMERCIAL PHOTOFLUOROGRAPHIC SCREENS

Brand	Resolving Power (lines per mm)
Patterson type 'B'	6
Patterson type 'D'	7
U S Radium and Chemical Co type 666 D	9

The resolving powers of three photo-fluorographic screens are listed in Table II. It will be observed that the screen produced by the U S Radium and Chemical Co is somewhat superior in this respect to the Patterson screens. All three screens

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Patterson Detail	17 $\frac{1}{2}$

cerned, for any given pair of intensifying screens the detail will be the same regardless of the type of film used

The maximum number of lines per millimeter which can be resolved by a film or film-screen combination is called resolving power. Most film-screen combinations now available to the radiologist have resolving powers of approximately 10 lines per millimeter, that is, the finest linear pattern which these combinations can resolve is one having 10 lines per millimeter. In general, resolving power measurements are an excellent index of the detail provided by various radiographic materials. During our preliminary experimental work, radiographs were made with a series of film-screen combinations on which resolving power measurements were made. These radiographs were made under conditions in which loss of detail due to movement of the part under examination and to target size were reduced essentially to zero. Differences, then, in the detail exhibited by the films were the result of differences in the characteristics of the screens themselves. The radiographs were submitted to a large number of radiologists, who were asked to place the films in their order of diagnostic merit. In almost every instance the radiologists' evaluations corresponded to the quantitative resolving power measurements. Only in those instances where two film-screen combinations had almost identical resolving powers were there discrepancies, and even here the radiologist frequently stated that there was no practical difference between the two combinations.

The resolving powers of eight commer-

cially available intensifying screens are shown in Table I. It will be observed that the screens designated as high-speed by various manufacturers generally have slightly lower resolving powers than those marked mid-speed and that the mid-speed screens in turn are slightly poorer than the screens listed as high-definition. With one exception (Patterson Detail screens), however, the difference between the poorest high-speed screen and the best high-definition screen is phenomenally small. Indeed, the difference between the detail provided by screens having a resolving power of 9 lines per millimeter and those having a resolving power of 12 $\frac{1}{2}$ lines per millimeter is hardly perceptible. This fact may seem strange to many radiologists, because almost everyone can remember a time when it was not difficult to differentiate so-called high-definition screens from so-called high-speed screens from the standpoint of detail. However, with the exception of Patterson Detail screens, all of the present-day brands, regardless of designation, provide about the same detail.

The resolving power of the Patterson type "B" fluoroscopic screen is 6 lines per millimeter. This value may appear unusually high to many readers in view of the rather poor detail which can be seen under fluoroscopic conditions. This poor detail, however, is not the fault of the screen but is due to the diminished visual acuity of the observer at the low levels of illumination occurring in fluoroscopy.

TABLE II RESOLVING POWER RATINGS OF COMMERCIAL PHOTOFLUOROGRAPHIC SCREENS

Brand	Resolving Power (lines per mm)
Patterson type B'	6
Patterson type D'	7
U S Radium and Chemical Co type 666 D	9

The resolving powers of three photo-fluorographic screens are listed in Table II. It will be observed that the screen produced by the U S Radium and Chemical Co is somewhat superior in this respect to the Patterson screens. All three screens

Characteristics of X-Ray Films and Screens¹

RUSSELL H MORGAN, M.D.

Baltimore, Md

MOST ROENTGENOLOGISTS have long recognized the need of reliable quantitative data giving the speed, detail, and contrast characteristics of commercially available roentgenographic films and intensifying screens. From such information, the choice of the most satisfactory films and screens for use in a roentgenographic department may be greatly facilitated. Furthermore, the availability of such information to the profession would constantly stimulate the x-ray industry to improve the quality of its products.

Before quantitative data listing the characteristics of films and screens can be made generally available to the radiologist, however, four fundamental steps must be taken. First, standard definitions of speed, detail, and contrast must be established. The terms of these definitions, of course, should correspond as closely as possible to the conditions which occur when the films and screens are used in normal roentgenographic practice. Second, methods of measurement which comply with the standard definitions must be developed. Third, an impartial and able laboratory to carry out such measurements must be set in operation. Fourth, the data must be published at regular intervals in journals that have a wide circulation among radiologists.

During the past year, the laboratory of the Radiology Section, U S Public Health Service, has been engaged in investigations from which standard definitions and methods of measurement of the various film and screen characteristics may be derived. Much of this research has been completed and has been reported in previous publications (1) or publications now in prepara-

tion. It is hoped that before long quantitative data on the characteristics of all x-ray films and screens will be published regularly in the two leading radiological journals of this country.

Before these data become generally available, it may be of interest to many to observe some of the preliminary results. Measurements have been made of the detail provided by eight types of intensifying screens, one fluoroscopic screen, and several of the screen-lens-film combinations which are used in photofluorography. Data have also been derived for the contrast factors of several photofluorographic films. We are not prepared to issue any speed data on various radiographic materials at this time, since our apparatus for making these measurements has just recently been completed.

DETAIL

The ability to record detail is measured in our laboratory by determining the finest linear pattern which can be resolved by a film or film-screen combination. Most radiographic film-screen combinations are able to resolve patterns up to 10 lines per millimeter. Photofluorographic combinations, however, are generally much poorer, while films exposed to x-rays directly frequently are able to resolve patterns having 50 lines per millimeter. Indeed, the ability of films alone to record detail is so much superior to that of intensifying screens that in the case of a film-screen combination it is the intensifying screens which limit the overall ability of the combination in this respect. As a result, it makes little difference what brand of film is used in an intensifying screen exposure as far as detail is con-

¹ From the Department of Radiology, The Johns Hopkins Hospital and the Radiology Section, Tuberculosis Control Division, U S Public Health Service. Presented at the Thirty second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

screens to conclude without saying a word regarding the persistence characteristics of various photofluorographic screens. Persistence, or lag as it is sometimes called, is a phenomenon characterized by the emission of light by a screen after the termination of the x-ray exposure. Some screens, such as the Patterson type "D" screen, exhibit this characteristic to a marked degree, whereas the Patterson type "B" screen has only negligible persistence.

The effect of persistence is twofold in photofluorography. If it is marked, there will be a considerable fogging of the various radiographic images in the film roll. Also, the performance of automatic photoelectric timers may be considerably impaired.

The marked persistence of the type "D" screen is unfortunate, because otherwise this screen has several valuable characteristics. First, its resolving power is slightly better than the type "B" screen. Also, this screen emits blue light and, therefore, employs blue-sensitive films that can be processed in conventional x-ray dark rooms without changing the lighting conditions, in contrast to the yellow-sensitive films that are used with the type "B" screen.

During the past year, many attempts have been made to produce a blue-emitting screen having short persistence characteristics similar to those of the type "B" screen. As Van Allen (3) has recently reported, the U S Radium and Chemical Co has been successful in meeting this objective in their type 666-D screen listed in some of the tables in this article. From laboratory and field tests, this screen seems to have such excellent over-all properties, as well as low persistence values, that before long it will likely receive wide usage in combination with such films as the experimental Ansco emulsion mentioned in Table IV. Such a combination will not only provide superior speed and contrast but a reasonably good resolving power, an absence of annoying persistence effects, and the advantage that the films may be processed under ordinary darkroom conditions.

CONCLUSION

The foregoing are the data that have been collected by our laboratory up to the present time. During the next year, our program will be organized to permit a complete quantitative evaluation of the speed, contrast, and resolving power characteristics of all commercially available x-ray films and screens. This information, soon thereafter, will be published regularly for the guidance of radiologists everywhere.

Department of Radiology
Johns Hopkins Hospital
Baltimore 5, Md

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DISCUSSION

W Edward Chamberlain, M D (Philadelphia, Penna) Dr Morgan's paper is of tremendous practical importance, as is all of the work that he and his colleagues do. The thought that we may be receiving in the near future regular published statements regarding the qualities of x-ray films that are commercially available is very interesting.

For a great many years Dr Henny and I at Temple University have made our own determinations of the contrast and speed of various films available on the open market with some rather interesting results, which, however, we have never ventured to publish, feeling that to do so might perhaps suggest that we were interested in selling a particular product.

I am interested to know what the reaction is going to be when we see set forth in print the differences which we have all observed in the laboratory. After all, the tendency will be for buyers to go rushing from one film to another, because there are very real differences. Every once in a while, we find one particular film standing out quite definitely above all others in the combination of speed and contrast.

A mention of the method we have used for determining some of these factors may be of interest. If you have an x-ray machine organized so that you can measure accurately its output and if you can maintain the quality of the beam constant—and it is not too hard to do that—then you can make, at any time you please, an exposure of a film enclosed be-

provide essentially the same speed when used with currently available photofluorographic films. However, Ansco is preparing to place in production a film for use with the Patterson type "D" and the U S Radium and Chemical Co type 666-D that will provide almost double the speed of the type "B" screen-film combination.

The ratings listed in Table II, of course, do not provide a reliable index of the detail visible in photofluorographic films, since the lens of the photofluorographic camera and the graininess of the film cause a considerable loss of detail. The over-all resolving powers of two photofluorographic combinations (screen, lens and film) are listed in Table III. One is for a 35-mm

TABLE III OVER-ALL RESOLVING POWER OF TWO PHOTOFLUOROGRAPHIC SYSTEMS (SCREEN CAMERA LENS AND FILM)

Type of System	Resolving Power (lines per mm)
Patterson type B' screen plus Eastman Ektar f/1.5 lens plus Eastman yellow sensitive 35 mm film	2.0
Patterson type D' screen plus Eastman Ektar f/1.5 lens plus Eastman blue sensitive 70 mm film	2.5

combination and the other for a 70-mm combination. It will be observed that the latter is only moderately better than the former. However, we have some evidence to indicate that if, in the 70-mm combination, a Patterson type "B" screen were used with an Eastman yellow-sensitive photofluorographic film, a resolving power approaching 3.0 lines per millimeter may be obtained. This higher resolving power is due to the smaller grain size of Eastman's yellow-sensitive film as compared to its blue-sensitive emulsion. A significant improvement in the resolving power of the 70-mm combination may also be accomplished by the replacement of the Patterson type "D" screen by the type 666-D screen of the U S Radium and Chemical Co. The higher resolving power of the latter screen will do much to counteract the loss of resolving power introduced by the many blue-sensitive emulsion.

TABLE IV CONTRAST RATINGS (GAMMA) OF FIVE PHOTOFLUOROGRAPHIC FILM SCREEN COMBINATIONS

Film Screen Combination	Contrast (Gamma)
Patterson type B' screen plus Eastman yellow sensitive P F film	1.6
Patterson type D' screen plus Eastman blue sensitive P F film	1.4
U S Rad & Chem Co type 666 D screen plus Eastman blue sensitive P-F film	1.6
Patterson type 'D' screen plus Ansco experimental P F film	1.8
U S Rad & Chem Co type 666-D screen plus Ansco experimental P F film	2.0

CONTRAST

Contrast ratings have been determined for five photofluorographic film-screen combinations. These data, listed in Table IV, were determined by measuring the maximum slopes of density vs log exposure curves made experimentally on the several combinations. They represent, therefore, what is usually referred to in the field of photography as gamma ratings. It is interesting to note that the contrast rating of the Patterson type "D" screen-Eastman blue-sensitive film combination is almost 15 per cent lower than that of the Patterson type "B" screen-Eastman yellow-sensitive film combination. In actual practice, the superiority of the latter combination is even greater than indicated, for it has been shown by recent work (2) that the x-ray contrast of images recorded by the type "B" screen is almost 10 per cent greater than that of the type "D" screen. As a result of the marked difference in over-all contrast between the two combinations, most radiologists quickly express a preference for films made with the type "B" screen-yellow-sensitive film combination. However, it will be noted from Table IV that there will soon be available photofluorographic film-screen combinations of the blue-sensitive type that will even surpass the contrast characteristics of any previous combination.

PERSISTENCE OF PHOTOFLUOROGRAPHIC SCREENS

It would be unwise in this discussion of the characteristics of x-ray films and

screens to conclude without saying a word regarding the persistence characteristics of various photofluorographic screens. Persistence, or lag as it is sometimes called, is a phenomenon characterized by the emission of light by a screen after the termination of the x-ray exposure. Some screens, such as the Patterson type "D" screen, exhibit this characteristic to a marked degree, whereas the Patterson type "B" screen has only negligible persistence.

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Department of Radiology
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Baltimore 5, Md

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A mention of the method we have used for determining some of these factors may be of interest. If you have an x-ray machine organized so that you can measure accurately its output and if you can maintain the quality of the beam constant—and it is not too hard to do that—then you can make, at any time you please, an exposure of a film enclosed be-

tween a particular pair of intensifying screens (carried, of course, in a particular cassette so as to eliminate differences in thickness and radiation absorption of various cassette covers), and then develop the film in a given developer for various lengths of time, and finally, with the densitometer determine exactly how much contrast is produced by the particular combination of film, developer, and intensifying screen used. Our method involves some differences in detail but not in principle from what Dr Morgan has shown us.

I should like Dr Morgan in his closing remarks to comment upon the problem of just what the commercial effects of these published statements will be. I think it takes some courage to start putting them in print and yet of course we are glad that it is going to be done.

In closing I want to ask Dr Morgan a couple of specific questions. When can we expect the new Ansco P-F film to be available? And is the United States Radium and Chemical Company 666-D Screen now available? If so, where and how do we obtain it. I think you all feel as I do. Those of you who have worked with P-F films realize that there is something to be desired in the present combination of blue screen and blue sensitive film partly because of the persistence or lag in the screen

and partly because we'd like to have more contrast in our results.

Russell H Morgan, M.D. (closing) I will answer briefly Dr Chamberlain's questions.

First of all, he asked what reaction we expect from the x-ray industry in regard to the publication of quantitative information regarding screens and films. We have already had a chance to see what that would be. We have been publishing some of this material in various issues of *Public Health Reports*. This journal doesn't have a very wide distribution among radiologists but we have been using it as a method of exploring reaction among those who do get that journal from time to time, and all that I can say is that this reaction so far has been most favorable. The x-ray industry has been extremely co-operative with us in all of this work and I think that the whole thing will go very smoothly indeed.

As to the availability of the United States Radium Company's screen and also of the new Ansco film, the screen, I believe, will be available within a period of weeks. As far as the film is concerned, it will probably be a matter of not longer than one or two months. Accordingly I think that the quality of photofluorographic films should take a marked step forward soon after the turn of the year.

SUMARIO

Características de las Películas y las Pantallas Roentgenológicas

Preséntanse datos relativos a la facultad resolvente, que constituye un índice de la capacidad para reproducir detalles, de 8 pantallas intensificadoras y 3 pantallas fotorroentgenográficas obtenibles en el mercado. También se suministran los coeficientes de comparación determinados para

5 combinaciones fotofluorográficas de película-pantalla. Por fin, se discute la "persistencia," es decir, la emisión de luz después de terminar la exposición a los rayos X, de varias pantallas fotorroentgenográficas.



Elastic Ruler for Roentgen Pelvimetry¹

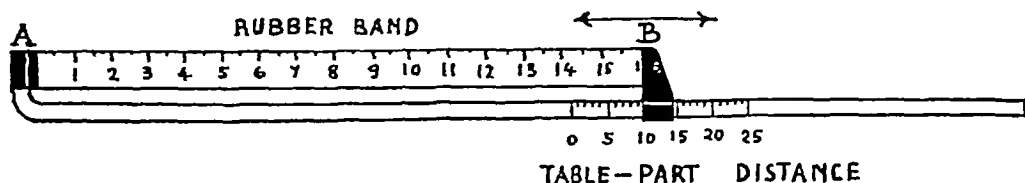
CESARE GIANTURCO, M D

Urbana, Ill

ELASTIC rulers have found use in radiology for the determination of the position of the pineal gland. They can also be used to good advantage to simplify roentgen pelvimetry.

The figure below shows an elastic ruler consisting of a metal rod bent at one end (A) and carrying a movable piece (B). A rubber band is fastened to A and B.

will be 11 mm instead of 10 mm. The rubber band is then stretched so that its length corresponds to the shadow of the 16 cm rod placed 5 cm above the table top and the new position of the movable piece is marked on the metal shaft. This is repeated for the rods placed at 10, 15, 20, 25 cm above the table top, and new marks are made on the shaft for each



By moving B, the rubber band can be stretched and held at any point along the shaft. The original length of the rubber band is 14 cm. After stretching it to 16 cm, 16 centimeter lines are marked on it.

Let us now take six metal rods, all 16 cm long, and place them on the x-ray table supported by radiolucent material so that one rod will be at table top level, and the others at 5, 10, 15, 20, and 25 cm above the table top. A film of these six rods is then taken with Bucky and with the film-tube distance that one intends to use for pelvimetry.² This film is placed on an illuminator and the rubber band is stretched so that its length will correspond to the shadow of the 16 cm rod placed on the table top. The position of the movable piece (B) is now marked on the metal shaft. Assuming that the shadow of the 16 cm rod placed on the table top becomes 17.6 cm when it reaches the film in the Bucky, the rubber band will distribute this increase over its entire length so that the distance between centimeter marks

position of the movable piece (B). The spaces between marks are then further divided into five equal spaces, each of which represents one centimeter of table top-part distance.

Once this is done, pelvimetric measurements become extremely simple. One anteroposterior axial film and one lateral film are taken, and the distance in centimeters between the table top and the inlet and the distance between the table top and the sagittal plane of the patient are noted.

The anteroposterior axial film is measured with the ruler set at first for the table top-inlet distance. At this setting, one can measure the true conjugate, the fetal head, the transverse diameter, and the two oblique diameters. A setting of 4 cm will measure accurately enough the interspinous diameter, and a setting of 15 cm the bi-ischial.

On the lateral film, one must set the instrument for the distance between the table top and the sagittal plane of the patient. This setting will serve for the true

¹ Accepted for publication in October 1946.

In this method as well as in other methods of pelvimetry, accuracy will be increased by the use of a long tube-film distance.

conjugate, the pubosacral diameter, and the fetal head

As long as the tube-film distance is kept constant, the measurements obtained with the elastic ruler are quite as accurate as those obtained by other methods. The

advantages of the method rest in its simplicity, in the economy of time and materials, and in the fact that measurements can be easily obtained on wet films

Carle Hospital Clinic
Urbana, Ill

SUMARIO

Regla Elástica para la Pelvimetría Roentgenológica

Descríbese una regla elástica para empleo en pelvimetría, cuyas ventajas comprenden sencillez, ahorro de tiempo y material y facilidad para hacer mediciones en películas húmedas



Vagotomy in the Treatment of Peptic Ulcer

The therapy of peptic ulcer has passed through numerous stages but has never been established on an entirely satisfactory basis. Treatment has included various types of medical management with alkalization as the basic factor and such surgical procedures as gastro-enterostomy, local excision of the ulcer, and more recently partial gastrectomy. Associated with all of these measures are certain disadvantages which have prevented their universal acceptance as an ideal method of treatment.

In 1943, Dragstedt and Owens (2) reported their experience with supradaphragmatic vagotomy in two cases of duodenal ulcer. This procedure they based upon the concept that such ulcers are attributable to the corrosive action of the gastric juice, excessive secretion of which may be due to hyperactivity of the gastric secretory fibers of the vagus nerves. In both cases satisfactory results were achieved.

This communication was followed in 1944 by a more detailed study by Dragstedt, Palmer, Schafer, and Hodges (3), of 11 patients with gastric and duodenal ulcers similarly treated. In this paper the authors discuss at some length the relation of gastric secretion to ulcer formation. They cite the work of Carlson, who showed that even in the fasting state and in the absence of psychic stimuli there is normally a more or less continuous secretion of gastric juice. What causes this is unknown, but it is assumed to be due, at least in part, to a persistent secretory tonus of the vagi. Under normal conditions, the gastric wall is not digested because it is not exposed to pure gastric juice for long periods but is protected by the intro-

duction of food. The pancreatic juice, gastric and intestinal mucus, duodenal juice, and bile offer further protection to the duodenum and to a less extent to the gastric and jejunal mucosa. When, however, excessive volumes of gastric juice are secreted continuously in experimental animals, especially in the absence of food, this defensive mechanism is overcome and an ulcer is produced. In a considerable number of ulcer patients there is also evidence of excessive production of gastric juice in the absence of any obvious stimulant, as at night when the stomach has been previously emptied of food by lavage. Follow-up observations of the 11 patients treated by Dragstedt and his associates by vagus section showed a striking decrease of this high night secretion following the operation, the reduction in most cases being in excess of 50 per cent. Associated with this there was persistent relief of ulcer pain and distress.

The observations recorded above were supplemented by physiological studies by Thornton, Storer, and Dragstedt (8) to determine the effect of vagotomy on the gastric secretory response to histamine, caffeine, insulin hypoglycemia, and a "sham meal" in which food was chewed but not swallowed. The increase in the volume of gastric secretion and free acid regularly produced by histamine and by caffeine was unchanged following vagotomy, indicating that the action of these stimulants is probably directly upon the gastric glands. On the other hand, the increase in secretion normally observed in the presence of insulin hypoglycemia and following a sham meal was completely abolished in vagotomized patients, confirming observations of others that these agents act through

stimulation of the gastric secretory fibers of the vagi. The absence of a secretory response to insulin or a sham meal is therefore suggested as a good test of the completeness of section of the vagal fibers.

A clinical study of 50 chronic ulcer cases treated by transthoracic vagotomy has recently been reported by Smith, Ruffin, and Baylin (7). All the patients in this series had chronic or recurrent ulcers which had failed to respond to previous medical or surgical measures, with symptoms ranging in duration from two to thirty-five years. Complete clinical recovery was obtained in 43 cases and the patients were able to return to a full, unrestricted diet. There was one questionable recurrence and one postoperative death. Five patients were relieved of ulcer symptoms but suffered from gastric retention, vomiting, persistent diarrhea, weakness, nervousness, or other symptoms. In this series, as in other reported series, the most common and serious postoperative complication was gastric retention associated with dilatation and hypoperistalsis, occasionally necessitating a secondary operation for relief. When a previous gastro-enterostomy had been done, no such difficulty was encountered. Diarrhea occurred in 27 patients but in 19 it was of only a few days' duration. Transient chest pain and fluid in the pleural cavity were minor complications.

Roentgen studies on this series of patients showed varying degrees of obstruction, the six-hour gastric residue ranged from 100 per cent to almost none. The duodenal bulb was frequently difficult to visualize. No point tenderness was present in most cases. The majority of the ulcers showed roentgen evidence of healing within several weeks or months.

Postoperative observations have also been reported from Massachusetts General Hospital, by Moore, Chapman, Schulz, and Jones (6), whose experience with vagotomy in ulcer cases covers two years. Of their 40 patients, 33 were followed long enough for an evaluation of progress. In 32 of these cases there was healing of

the original ulcer but in 2 cases pain continued and in one a late gastro-enterostomy was required. Of the 29 patients classified as showing satisfactory results, there were 3 who had diarrhea persisting from three to five months, and 2 others with postprandial symptoms of epigastric pressure and faintness. The diarrhea ceased spontaneously in all cases, but one patient still complained of postprandial distress after two years. No recurrences have been encountered in this series.

Attempts are being made to overcome the complication of gastric retention with lack of tone and decreased peristaltic activity. Machella, Hodges, and Sorber (4) gave urethane of B-methyl choline chloride to two patients with disturbances of the motor function of the stomach following bilateral vagotomy for ulcer, and showed by roentgenologic and balloon kymographic studies that the parenteral introduction of this drug temporarily restored gastric peristalsis and motility with relief of epigastric distress, anorexia, and nausea. A side effect of this was an increase in gastric acid secretion in the fasting stomach, which may or may not be detrimental to ulcer healing.

It is known that in a certain number of cases the vagi do not consist of two main trunks but divide and form a plexus in their lower course. This has caused some uncertainty concerning the proper site for section of the nerves. Dragstedt in his earlier cases, and most of the authors quoted above, have used the supradiaphragmatic route to insure section of all the nerve fibers. This, however, precludes visual and manual observation of the lesion under treatment, and thus allows for the possibility of an incorrect diagnosis. Recently Dragstedt has switched to the transabdominal approach in order to have the additional advantage of inspection of the ulcer. Differences of opinion as to the comparative effectiveness of the two procedures remain to be settled. As a result of an anatomic study of the vagus nerves at the postmortem table Bradley, Small,

Wilson, and Walters (1) believe that in more than 90 per cent of cases, a subdiaphragmatic approach will allow as nearly a complete division of all the nerve fibers as a transthoracic approach. Miller and Davis (5), however, as a result of a similar study, strongly favor the supradiaphragmatic approach, feeling that otherwise some of the nerve branches may be missed.

The preliminary reports on vagotomy in the treatment of peptic ulcer are encouraging, but the interval since its introduction is short. A much longer time will be required to evaluate fully the place of this procedure in ulcer therapy. It represents primarily a physiologic approach to the problem and should stimulate further physiologic studies to determine finally the effect not only on the stomach but on the other abdominal organs. The immediate relief of ulcer symptomatology is dramatic, but the subsequent gastric atony and delay in motility occasionally observed may be very distressing, although in most cases these after effects eventually disappear. The volume and acidity of the gastric juice are significant factors in the production of peptic ulcer. Vagotomy done

in connection with partial gastrectomy would appear to be of definite value in modifying gastric secretion and thus acting to prevent the development of gastrojejunal ulcers frequently observed as a complication of the latter operation.

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An Announcement Publication of Spanish Summaries

With this issue, RADIOLOGY embarks upon a new undertaking, which it is anticipated will greatly increase its usefulness, namely, the publication of summaries in Spanish of all original contributions appearing in its pages.

Barriers of language have never been effective in halting the advance of scientific achievement, but that they may hinder the prompt exchange of useful experiences is undeniable. We believe that Latin American radiologists will welcome the opportunity to follow, month by month, the work of their North American colleagues, while our own interest in the contributions of Latin America to our common

specialty will be enhanced by the closer relationship thus established.

If proof were needed of the international character of the science of radiology and the community of interest existing among radiologists of the Americas, it was amply demonstrated by the recent Inter-American Congress of Radiology at Havana and the action there taken toward the establishment of an Inter-American College of Radiology. It is our hope that the new policy of making available in Spanish the substance of our current publications will be yet another bond between radiologists of the Western Hemisphere.

Publicacion de Sumarios en Español

Con la esperanza de que acreciente considerablemente su utilidad, sobre todo en la América Latina, RADIOLOGY lanza, con este número, una innovación, o sea, la publicación en castellano de sumarios de todos los trabajos originales que aparezcan en sus páginas

Las vallas del lenguaje jamás han logrado contener el adelanto científico, pero tampoco cabe negar que pueden impedir el rápido intercambio de conocimientos útiles. A nuestro parecer, los radiólogos latino-americanos acogerán con placer la oportunidad de seguir, en su propio idioma, de mes en mes, la labor de sus colegas del Norte, en tanto que nuestro propio interés en los aportes latino-americanos a nuestra

mutua especialidad se verá avivado por las relaciones más íntimas así establecidas

Si se necesitara mayor prueba de la naturaleza internacional de la ciencia radiológica y de la mutualidad de intereses que existe entre los radiólogos de las Américas, bien amplia la ofreció el reciente Congreso Inter-Americano de Radiología celebrado con tanta brillantez en la Habana y la decisión allí tomada con respecto al establecimiento de un Colegio Inter-Americano de Radiología. Abrigamos la sincera esperanza de que la nueva política de presentar en español la sustancia de nuestros trabajos corrientes forje otro lazo de unión entre los radiólogos del Hemisferio Occidental



ANNOUNCEMENTS AND BOOK REVIEWS

PRESENTATION TO DR R S STONE

For reasons metallurgical, the Gold Medal of the Radiological Society of North America awarded to Dr R S Stone was not ready for presentation at the time of the Annual Meeting of the Society last December. It was completed in the spring of this year, and the Secretary of the Society suggested to the President-Elect that, since he resided in the same city as Dr Stone, he present the medal at some suitable occasion. The latter was kindly arranged at a meeting of Dean Smith, of the University of California Medical School, and Dr Childs.

Accordingly, at the May 24, 1947, Faculty Meeting of the University of California Medical School, the award was made, with the following remarks by Dr L H Garland.

"Gentlemen. It is a high privilege indeed to come before the faculty of the Medical School of the University of California with this so pleasant task.

"The Gold Medal of the Radiological Society of North America has not been awarded since 1941. Its prior recipients include many distinguished physicians and physicists, amongst whom one recollects Gösta Forssell, Madame Curie, Maud Slye, Arthur Compton, Robert Millikan, Edith Quimby, and others. These names are lustre in the quiet halls of science, and shed a glow of brilliance in our world. To this outstanding group is added now the name of Robert Stone, your professor of radiology. His academic standing, like his modesty, bears the stamp of greatness.

"As Associate Director of Health for the Metallurgical Project he bore a grave responsibility with courage, competence, and silence. The work he did involved uprooting ties with home and school, much travel, no small personal danger and, above all, the discipline of everlasting secrecy.

"Robert Spencer Stone, on behalf of the Radiological Society of North America, and through it, of the radiologists of the New World, it is my privilege, as President-Elect of that Society, to bestow on you its Gold Medal.

'May I conclude with Robinson Jeffers words
*Lend me the stone strength of the past and I will
lend you*

The wings of the future, for I have them'

"It is my fortune to call you comrade."

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

The Mid summer Conference of the Rocky Mountain Radiological Society will be held at the Shirley Savoy Hotel, Denver, Colo., August 7, 8, and 9, 1947. The program is not complete, but two of the guest speakers will be Dr Lowell S Goin, Los Angeles, Calif., and Dr Leo G Rigler, Minneapolis, Minn. There will be other guest speakers. It is suggested that radiologists plan their vacations to attend this conference.

FOURTH INTERNATIONAL CANCER RESEARCH CONGRESS

The Fourth International Cancer Research Congress, sponsored by Union Internationale Contre le Cancer and the American Association for Cancer Research, with the assistance of other organizations and individuals interested in promoting cancer research, will be held in St. Louis, Mo., Sept 2-7, 1947, with headquarters at the Jefferson Hotel. Dr E V Cowdry of the Barnard Free Skin and Cancer Hospital, St. Louis, is the Chairman of the Executive Committee, Dr Shields Warren, Boston, of the Program Committee, and Dr G W Larimore of the American Cancer Society (47 Beaver St., New York) of the Exhibits Committee. The local arrangements are in the hands of a committee headed by Dr A N Arneson of the Mallinckrodt Institute of Radiology, St. Louis.

For room reservations application should be made promptly to Mr F H Rein, St. Louis Publicity and Convention Bureau, 911 Locust St., St. Louis 1, Mo.

AMERICAN CONGRESS OF PHYSICAL MEDICINE

The American Congress of Physical Medicine will hold its twenty-fifth annual scientific and clinical session Sept 2-6, inclusive, at the Hotel Radisson, Minneapolis. Scientific and clinical sessions will be given on the days of Sept 3, 4, 5, and 6. In addition to the scientific sessions, the annual instruction courses will be held Sept 2, 3, 4, and 5. For information concerning the convention and the instruction courses, address the American Congress of Physical Medicine, 30 North Michigan Avenue, Chicago 2, Ill.

RADIOLOGICAL SOCIETIES SECRETARIES AND MEETING DATES

Editor's Note Secretaries of state and local radiological societies are requested to cooperate in keeping this section up-to date by notifying the editor promptly of changes in officers and meeting dates Address Howard P. Doub, M.D., The Henry Ford Hospital Detroit 2 Mich

UNITED STATES

RADIOLOGICAL SOCIETY OF NORTH AMERICA *Secretary Treasurer*, Donald S. Childs M.D. 607 Medical Arts Bldg., Syracuse 2, N.Y.

AMERICAN RADIUM SOCIETY *Secretary* Hugh F. Hare, M.D., 605 Commonwealth Ave. Boston 15 Mass

AMERICAN ROENTGEN RAY SOCIETY *Secretary* Harold Dabney Kerr M.D. Iowa City, Iowa

AMERICAN COLLEGE OF RADIOLOGY *Secretary*, Mac F. Cahal 20 N. Wacker Dr., Chicago 6 Ill

SECTION ON RADIOLOGY, A.M.A. *Secretary* U.V. Portmann, M.D., Cleveland Clinic, Cleveland 6, Ohio

Alabama

ALABAMA RADIOLOGICAL SOCIETY *Secretary-Treasurer* Courtney S. Strickley, M.D. Bell Bldg. Montgomery Next meeting at the time and place of the Alabama State Medical Association meeting

Arkansas

ARKANSAS RADIOLOGICAL SOCIETY *Secretary*, Fred Hames, M.D., Pine Bluff Meets every three months and annually at meeting of State Medical Society

California

CALIFORNIA MEDICAL ASSOCIATION, SECTION ON RADIOLOGY *Secretary*, D.R. MacColl M.D., 2007 Wilshire Blvd. Los Angeles 5

LOS ANGELES COUNTY MEDICAL ASSOCIATION, RADIOLOGICAL SECTION *Secretary* Morris Horwitz, M.D., 2009 Wilshire Blvd., Los Angeles 5 Meets second Wednesday of each month at County Society Bldg

PACIFIC ROENTGEN SOCIETY *Secretary* L. Henry Garland M.D., 450 Sutter St. San Francisco 8 Meets annually with State Medical Association

SAN DIEGO ROENTGEN SOCIETY *Secretary* R.F. Niehaus M.D. 1831 Fourth Ave. San Diego Meets first Wednesday of each month

X-RAY STUDY CLUB OF SAN FRANCISCO *Secretary* Ivan J. Miller M.D. 2000 Van Ness Ave. Meets monthly on the third Thursday at 7:45 P.M. January to June at Lane Hall Stanford University Hospital and July to December at Toland Hall, University of California Hospital

Colorado

DENVER RADIOLOGICAL CLUB *Secretary* Washington C. Huyler, M.D. Mercy Hospital 1619 Milwaukee Denver 6 Meets third Friday of each month at the Colorado School of Medicine and Hospitals

Connecticut

CONNECTICUT STATE MEDICAL SOCIETY SECTION ON RADIOLOGY *Secretary* Robert M. Lowman M.D. Grace-New Haven Hospital Grace Unit New Haven Meetings bimonthly second Thursday

Florida

FLORIDA RADIOLOGICAL SOCIETY *Secretary Treasurer* Maxey Dell Jr., M.D., 333 West Main St. S Gainesville

Georgia

GEORGIA RADIOLOGICAL SOCIETY *Secretary Treasurer* Robert Drane M.D., De Renne Apartments Savannah Meets in November and at the annual meeting of State Medical Association

Illinois

CHICAGO ROENTGEN SOCIETY *Secretary* T.J. Wachowski, M.D. 310 Ellis Ave., Wheaton Meets at the Palmer House, second Thursday of October November January, February March, and April at 8:00 P.M.

ILLINOIS RADIOLOGICAL SOCIETY *Secretary Treasurer* William DeHollander, M.D., St. John's Hospital Springfield Meetings quarterly as announced

ILLINOIS STATE MEDICAL SOCIETY SECTION ON RADIOLOGY *Secretary*, Frank S. Hussey M.D., 250 East Superior St. Chicago-11

Indiana

INDIANA ROENTGEN SOCIETY *Secretary Treasurer*, J.A. Campbell, M.D. Indiana University Hospitals Indianapolis 7 Annual meeting in May

Iowa

IOWA X-RAY CLUB *Secretary* Arthur W. Erskine M.D., 326 Higley Building Cedar Rapids Meets during annual session of State Medical Society

Kentucky

KENTUCKY RADIOLOGICAL SOCIETY *Secretary Treasurer* Sydney E. Johnson M.D. 101 W. Chestnut St., Louisville

LOUISVILLE RADIOLOGICAL SOCIETY *Secretary Treasurer* Everett L. Pirkey Louisville General Hospital Louisville 2 Meets second Friday of each month at Louisville General Hospital

Louisiana

LOUISIANA RADIOLOGICAL SOCIETY *Secretary Treasurer* Johnson R. Anderson M.D. No. Louisiana Sanitarium Shreveport Meets with State Medical Society

ORLEANS PARISH RADIOLOGICAL SOCIETY *Secretary*, Joseph V Schlosser, M D, Charity Hospital of Louisiana, New Orleans 13 Meets first Tuesday of each month

SHREVEPORT RADIOLOGICAL CLUB *Secretary*, Oscar O Jones M D 2622 Greenwood Road Meets monthly September to May, third Wednesday, 7 30 P M

Maryland

BALTIMORE CITY MEDICAL SOCIETY RADIOLOGICAL SECTION *Secretary-Treasurer*, Harry A Miller, M D 2452 Eutaw Pl, Baltimore

Michigan

DETROIT X RAY AND RADIUM SOCIETY *Secretary Treasurer* E R Witwer, M D Harper Hospital, Detroit 1 Meetings first Thursday of each month from October to May at Wayne County Medical Society club rooms

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS *Secretary Treasurer* R B MacDuff M D, 220 Genesee Bank Building, Flint 3

Minnesota

MINNESOTA RADIOLOGICAL SOCIETY *Secretary* C N Borman M D 802 Medical Arts Bldg Minneapolis 2 Regular meetings in the Spring and Fall

Missouri

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY *Secretary* John W Walker, M D 306 E 12th St., Kansas City Mo Meetings last Friday of each month

ST LOUIS SOCIETY OF RADIOLOGISTS *Secretary*, Edwin C Ernst M D, 100 Beaumont Medical Bldg Meets on fourth Wednesday of each month, October to May

Nebraska

NEBRASKA RADIOLOGICAL SOCIETY *Secretary Treasurer* O A Neely, M D 924 Sharp Building Lincoln Meetings third Wednesday of each month at 6 P M in either Omaha or Lincoln

New England

NEW ENGLAND ROENTGEN RAY SOCIETY *Secretary-Treasurer*, George Levene M D, Massachusetts Memorial Hospitals Boston Mass Meets monthly on third Friday at Boston Medical Library

New Hampshire

NEW HAMPSHIRE ROENTGEN SOCIETY *Secretary-Treasurer* Albert C Johnston M D Elliot Community Hospital Keene Meetings quarterly in Concord

New Jersey

RADIOLOGICAL SOCIETY OF NEW JERSEY *Secretary*, W H Seward M D Orange Memorial Hospital

Orange. Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called

New York

ASSOCIATED RADIOLOGISTS OF NEW YORK, INC *Secretary*, William J Francis, M D, East Rockaway, L I

BROOKLYN ROENTGEN RAY SOCIETY *Secretary Treasurer*, Abraham H Levy, M D, 1354 Carroll St, Bklyn 13 Meets fourth Tuesday of every month, October to April

BUFFALO RADIOLOGICAL SOCIETY *Secretary Treasurer*, Mario C Gian M D, 610 Niagara St, Buffalo 1 Meetings second Monday evening each month, October to May, inclusive

CENTRAL NEW YORK ROENTGEN SOCIETY *Secretary-Treasurer*, Dwight V Needham, M D, 608 E Genesee St, Syracuse 10 Meetings in January, May and October

LONG ISLAND RADIOLOGICAL SOCIETY *Secretary*, Marcus Wiener, M D, 1430 48th St, Brooklyn 19 Meetings fourth Thursday evening each month at Kings County Medical Bldg

NEW YORK ROENTGEN SOCIETY *Secretary*, Wm Snow, M D 941 Park Ave, New York, 28

ROCHESTER ROENTGEN RAY SOCIETY *Secretary* Murray P George, M D, 260 Crittenden Blvd, Rochester 7 Meets at Strong Memorial Hospital third Monday September through May

North Carolina

RADIOLOGICAL SOCIETY OF NORTH CAROLINA *Secretary Treasurer*, James E Hemphill M D Professional Bldg, Charlotte 2 Meets in May and October

North Dakota

NORTH DAKOTA RADIOLOGICAL SOCIETY *Secretary*, Charles Heilman M D, 1338 Second St N, Fargo

Ohio

OHIO RADIOLOGICAL SOCIETY *Secretary*, Henry Snow, M D, 1061 Reibold Bldg Dayton 2 Next meeting at annual meeting of the Ohio State Medical Association

CENTRAL OHIO RADIOLOGICAL SOCIETY *Secretary*, Hugh A Baldwin M D, 347 E State St Columbus

CLEVELAND RADIOLOGICAL SOCIETY *Secretary-Treasurer*, George L Sackett, M D 10515 Carnegie Ave Cleveland 6 Meetings at 6 30 P M on fourth Monday, October to April, inclusive

RADIOLOGICAL SOCIETY OF THE ACADEMY OF MEDICINE (Cincinnati Roentgenologists) *Secretary-Treasurer* Samuel Brown M D, 707 Race St, Cincinnati 2 Meets third Tuesday of each month

Oklahoma

OKLAHOMA STATE RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Peter M Russo, M D, 230 Osler Building Oklahoma City Meetings three times a year

Pennsylvania

PENNSYLVANIA RADIOLOGICAL SOCIETY *Secretary*
Treasurer, James M Converse, M D, 416 Pine
 St., Williamsport 8 Meets annually

PHILADELPHIA ROENTGEN RAY SOCIETY *Secretary*,
 Calvin L Stewart, M D Jefferson Hospital,
 Philadelphia 7 Meets first Thursday of each
 month at 8 00 P M, from October to May in
 Thomson Hall, College of Physicians, 21 S 22d St

PITTSBURGH ROENTGEN SOCIETY *Secretary-Treasurer*,
 Lester M J Freedman, M D, 415 Highland Bldg.,
 Pittsburgh 6 Meets second Wednesday of each
 month at 6 30 P M October to May, inclusive

Rocky Mountain States

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY *Secretary-
 Treasurer*, A M Popma, M D, 220 N First St
 Boise Idaho

South Carolina

SOUTH CAROLINA X-RAY SOCIETY *Secretary-Treasurer*,
 Robert B Taft, M D 103 Rutledge Ave., Charles-
 ton 16

Tennessee

MEMPHIS ROENTGEN CLUB Meetings second Tuesday
 of each month at University Center

TENNESSEE RADIOLOGICAL SOCIETY *Secretary Treas-
 urer*, J Marsh Frère, M D, 707 Walnut St, Chat-
 tanooga Meets annually with State Medical
 Society in April

Texas

DALLAS FORT WORTH ROENTGEN STUDY CLUB *Sec-
 retary* X R. Hyde, M D, Medical Arts Bldg.,
 Fort Worth 2 Meetings on third Monday of each
 month, in Dallas in the odd months and in Fort
 Worth in the even months

TEXAS RADIOLOGICAL SOCIETY *Secretary Treasurer*,
 R P O'Bannon M D 650 Fifth Ave Fort Worth
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Utah

UTAH STATE RADIOLOGICAL SOCIETY *Secretary Treas-
 urer* M Lowry Allen M D Judge Bldg Salt
 Lake City 1 Meets third Wednesday January
 March, May September November

UNIVERSITY OF UTAH RADIOLOGICAL CONFERENCE
Secretary Henry H Lerner M D Meets first and
 third Thursdays, September to June, inclusive,
 at Salt Lake County General Hospital

Virginia

VIRGINIA RADIOLOGICAL SOCIETY *Secretary* E Latan
 Flanagan, M D, 215 Medical Arts Bldg Rich-
 mond 19

Washington

WASHINGTON STATE RADIOLOGICAL SOCIETY *Secre-
 tary Treasurer*, Frederic E Templeton M D, 324
 Cobb Bldg., Seattle 1 Meetings fourth Monday,
 October through May, at College Club, Seattle.

Wisconsin

MILWAUKEE ROENTGEN RAY SOCIETY *Secretary-
 Treasurer*, C A H Fortier, M D, 231 W Wiscon-
 sin Ave., Milwaukee 3 Meets monthly on second
 Monday at the University Club

RADIOLOGICAL SECTION OF THE WISCONSIN STATE MED-
 ICAL SOCIETY *Secretary*, S R. Beatty M D, 185
 Hazel St., Oshkosh Two-day meeting in May
 and one day at annual meeting of State Medical
 Society in September

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE
 Meets first and third Thursdays 4 to 5 P M, Sep-
 tember to May inclusive Room 301, Service Mem-
 orial Institute 426 N Charter St., Madison 6

CANADA

CANADIAN ASSOCIATION OF RADIOLOGISTS *Honorary
 Secretary Treasurer* E M Crawford M D, 2100
 Marlowe Ave Montreal 28 Quebec Meetings
 in January and June

LA SOCIÉTÉ CANADIENNE FRANÇAISE D'ELECTROLOGIE
 ET DE RADIOLOGIE MÉDICALES. *General Secretary*,
 Origène Dufresne, M D Institut du Radium
 Montreal Meets on third Saturday of each
 month

CUBA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA
 Offices in Hospital Mercedes Havana Meets
 monthly

MEXICO

SOCIEDAD MEXICANA DE RADIOLOGÍA Y FISIOTERAPIA
General Secretary Dr Dionisio Pérez Cosío
 Marsella 11 México D F Meetings first Monday
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ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Observations on Encephalographic Findings in Cerebral Trauma Charles E. Troland, Donald H. Baxter and Richard Schatzki J Neurosurg 3 390-398 September 1946

The encephalographic findings in a series of 261 patients (177 with head injuries with skull defects, 29 with closed head injuries, 32 with idiopathic epilepsy, 23 with other lesions of the central nervous system) are reviewed. The x-ray reports were available in all instances and the actual films were obtained for review and for special measurements in 193 cases, 159 of which were cases of head injury. Some of the clinical records were not at the authors' disposal at the time of the study. In all cases a complete series of roentgenograms consisting of anteroposterior, postero-anterior, and both lateral stereoscopic views was made. A description of the encephalographic technique used is included.

In the series of 261 encephalograms, satisfactory filling of the ventricles was shown in 227 (87.5 per cent), poor filling in 15 (5.5 per cent), and no filling in 19 (7 per cent). In 168 cases of all types the ventricular filling was satisfactory and the films were available for review. The encephalograms were abnormal in 117 of this group and normal in 51.

Of the 143 cases of head injury in which filling of the ventricles was satisfactory and the films and clinical records were available, 17 (12 per cent) showed a shift of the ventricular system toward the side of the cranial defect. In 12 (8.5 per cent) of the 143 cases there was symmetrical enlargement of the lateral and third ventricle. Two patients with non-traumatic epilepsy also showed this type of ventricular dilatation. It is thought that in the majority of cases this condition is due to generalized loss of cerebral substance with secondary dilatation of the cerebrospinal system. Eleven cases (8 per cent) revealed enlargement of both lateral ventricles without enlargement of the third ventricle. In 41 (29 per cent) bilateral asymmetrical enlargement of the lateral ventricles was evident of this number 31 (75 per cent) showed also dilatation of the third ventricle. The side of the greatest enlargement of the lateral ventricle was always the side of the injury in both open and closed head injuries. In 42 of the 143 instances (29 per cent) there was enlargement of only one lateral ventricle.

In a group of 60 patients in whom second day study of the ventricles was made, an increase in the ventricular size on the second day was found in over one third.

There were 126 cases of cranial trauma of both types in which the exact time of the injury was known and the encephalograms were excellent; in 33 (26 per cent) the injury had been sustained less than three months before encephalography and of these 20 (60 per cent) showed ventricular enlargement of some type.

Of 129 cases of cranial trauma in which filling of the ventricles was satisfactory and there was adequate neurologic information, 11 (8.5 per cent) revealed a normal ventricular system in the presence of clinical evidence of definite neurological damage. In 61 (47.5 per cent) there were positive evidence of neurological damage and abnormal encephalographic findings while 26 (20 per cent) had no clinical or encephalographic signs of cerebral damage. In 31 (24 per cent) the encephalo-

gram was abnormal, although the neurologic examination was negative.

In 123 cases (116 patients with cranial defects, 7 closed head injuries) encephalographic filling was satisfactory and information was available as to post-traumatic symptoms. Six of the 7 patients with closed head injuries had severe post-concussion syndromes consisting of headache, dizziness, intolerance to alcohol, and some loss of memory. Four of these had normal encephalograms. Of the 116 patients with cranial defects, 47 (41 per cent) had post-traumatic symptoms (headaches, dizziness, etc.), 14 (29 per cent) of these had normal encephalograms.

Encephalography has been said by many authors to relieve post-traumatic symptoms but in this series the amount of relief was meager and minimal.

Toxoplasmic Encephalomyelitis, with the Report of Two Cases E. Graeme Robertson M. J. Australia 2 449-452 Sept 28 1946

The protozoan parasite *Toxoplasma* produces various clinical manifestations, summarized by Sabin (in *Advances in Pediatrics*, New York: Interscience Publishers Vol I, 1942) as follows: (1) abnormal enlargement of the head *in utero*, the result of encephalomyelitis in the fetus; (2) encephalomyelitis of the newborn (originating *in utero*), which terminates fatally during the first days or weeks of life; (3) congenital encephalomyelitis giving rise to hydrocephalus or microcephaly, cerebral calcification, chorioretinitis, and nervous disturbances such as convulsions ('epilepsy'), spasticity, and mental deficiency observed in infancy and early childhood; (4) atypical encephalitis, with twitchings of isolated muscle groups, convulsions, disorientation, low-grade fever and pleocytosis but thus far without the so-called 'signs of meningeal irritation' (nuchal rigidity, Kernig's sign, etc.) and without signs pointing to involvement of the cranial nerves; (5) acute febrile exanthematic disease associated with atypical pneumonia; (6) a mild or inapparent infection betrayed only by the demonstration of antibodies against toxoplasma or the birth of an infant with clinically apparent toxoplasmosis.

The roentgen features in children have been described by Dyke *et al.* (*Am J Roentgenol* 47 830 1942; *Abst in Radiology* 41 84 1943). They consist chiefly in multiple small bilateral rounded areas of calcium density 1 to 3 mm in diameter in the brain substance. There may be curvilinear calcium streaks in the basal ganglia. Signs of hydrocephalus or microcephaly may be evident.

The author presents two cases with many of the salient features of the disease. The first patient, a girl of thirteen, developed normally for one and one half years and then began to show evidence of retarded mentality, unilateral microphthalmia, speech difficulty and poor vision which increased with advancing age. She complained of headaches, was unstable in her emotional responses and at the age of twelve began to have convulsive seizures limited to the left side. Radiographic examination of the skull showed widely scattered areas of calcification chiefly in the lower and outer parts of the parietal lobes, more pronounced on the right side. One small round mass was seen in the right frontal lobe. Symmetrical comma-shaped deposits were present in the region of the caudate nuclei. The

bones were thick and well marked digital impressions were seen in them. Encephalographic studies showed normal filling of the cisterna magna the fourth ventricle and the aqueduct but no filling of the third ventricle and the lateral ventricles. Additional air merely outlined the other basilar cisterns and the cerebral sulci which appeared normal. Treatment with phenobarbital and "Dilantin" abolished the epileptic manifestations and improved the temperament of the child.

The second patient showed rapid enlargement of the head for four days after birth, followed by more normal development. She was lethargic when first seen, but no clinical evidence of hydrocephalus was present. The left eye was smaller than the right and the media on this side were opaque, the pupil was irregular, the cornea was clouded and posterior synechiae were present. Choroiditis and posterior synechiae were present on the right. Roentgenograms of the skull revealed two faint crescentic areas of calcification apparently in the region of the basal ganglia. At the age of thirteen months the cephalic circumference was 17 5 inches. The eyes were unchanged. No abnormal neurological signs were present except evidence of delayed mental development. The calcifications observed radiographically appeared more dense but of the same distribution as before.

Though there was no definite proof obtained of toxoplasmic infection in either of these cases, the author believes the clinical syndrome together with the objective findings are sufficient to establish the diagnosis.

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If the conventional roentgenogram shows nothing abnormal it is important for the roentgenologist to emphasize the possibilities of air encephalography. The authors describe clearly the normal appearances of the cisternae chiasmatis, interpeduncularis and pontis and these are illustrated in the text. The carotid artery, the anterior communicating artery and occasionally the middle cerebral artery may be outlined in the superior portion of the cisterna chiasmatis. An ovoid shadow just above the sella turcica represents the optic chiasm. The infundibulum of the hypophysis is seen more posterior.

The encephalographic findings in optochiasmatic arachnoiditis are rather typical if the cerebrospinal

system is well drained of fluid, which is replaced with air through the lumbar route. The shadows of the cisternae chiasmatis and interpeduncularis can be readily demonstrated in most individuals who have no symptoms referable to that region. In the presence of optochiasmatic arachnoiditis the clear air shadows of the cisterna chiasmatis, and occasionally the cisternae interpeduncularis and pontis, are absent, deformed or encroached upon and the structures usually seen cannot be identified. Tumor is usually thought to be present. We now know that chiasmal arachnoiditis should always be considered in arriving at the final diagnosis.

Four cases of chiasmatic arachnoiditis, one of syphilitic origin, are presented. Pitfalls in diagnosis include errors in technique such as incomplete drainage and examination in the horizontal posture employing a vertical beam. Lesions such as tumor in the region of the optic chiasm are shown to illustrate the difficulty of differential diagnosis in some instances.

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One hundred apparently normal subjects in an army hospital gave the following measurements for the sella turcica: average anteroposterior diameter 10.66 mm., average depth, 8.30 mm. The largest sella measured 13 mm. (anteroposterior) by 9 mm. (depth) and the smallest 8 by 5 mm. Seven per cent of the series showed bridging of the sella. The usual contour was oval, 53 per cent, a round contour was present in 28 per cent while in 19 per cent the sella was either oblong or flat.

The author describes and illustrates many normal variants of the sella, the clinoids, the sphenoid sinus and the dorsum sellae. It is important that the roentgenologist be conversant with the numerous normal variants which may be encountered. Physiological calcification of the petroclinoid ligaments is a well known finding. Calcium deposits may be found within the pituitary gland and are not necessarily of clinical importance. Faint calcification above the fossa often indicates the presence of a Rathke's pouch tumor.

In the presence of a tumor, roentgen evidence usually precedes visual field involvement. Interpretation of the visual field findings usually throws some light on the severity of the damage done and degree of improvement following irradiation and surgery and offers as well a delicate means of evaluating the effectiveness of therapy. Choked disks are rarely seen with pituitary adenoma. Adenoma causes a uniform and general enlargement of the fossa, the ventral wall of the dorsum is smoothly eroded, the dorsum is often displaced posteriorly and apparently elongated. If eccentric in position the tumor may cause erosion of the ipsilateral anterior clinoid.

Any bizarre appearance of the hypophyseal fossa or a roentgen picture not consistent with diagnosis of adenoma should bring to mind some form of extrasellar lesion. Pressure transmitted from above due to a dilated third ventricle may erode the posterior clinoids and the dorsum. This may be the result of tumor or stricture of the aqueduct. A nasopharyngeal tumor is described which invaded the floor of the middle fossa in the left parasellar region. Carcinoma metastases and multiple myeloma have been known to invade the sella. Aneurysms of the circle of Willis will if large enough cause marked sellar deformation. Calcification in the

wall of the aneurysm is often seen on conventional roentgenograms. This must be differentiated from sclerosis without aneurysm. For accurate diagnosis the method of choice is arteriography.

CLARENCE E WEAVER M D

Roentgen Diagnosis of Clivus Chordoma Siegfried Epple and Ernst Ruckenstein Schweiz med Wchnschr 76 764-766 Aug 17 1946

Clivus chordomas occur at the base of the skull and are of two types benign and malignant. The latter do not tend to metastasize but are characterized by cranial nerve involvement most often of the abducens. Pressure on the brain stem may lead to pyramidal tract symptoms. Elevation of intracranial pressure is rare and occurs only late in the disease. Roentgenologic signs are few in the benign type exostotic like projections of bone in the region of the clivus have been described in contrast to which the malignant type destroys the clivus. Calcification in the tumor is exceptional. Filling of the nasal space may occur or of the retropharyngeal space with vertebral involvement. Air filling does not necessarily lead to a diagnosis since, as Lysholm has pointed out cerebellar tumors and chivus meningiomas produce similar pictures. The author records a case of the malignant type in a 57 year-old man in which roentgenograms showed destruction in the base of the skull and of the tip of the sphenoid.

LEWIS G JACOBS M D

Lückenschädel in a Patient with Amnesia Amenable to Hypnotherapy A Personality Study Jerome M Schneck J Nerv & Ment Dis 104 249-262 September 1946

A case of Lückenschädel in a boy of 18 with amnesia which proved amenable to hypnotherapy is presented. This is apparently the oldest patient with this condition reported thus far and probably only the second patient discussed in the literature who has lived beyond infancy. The literature is reviewed and roentgenograms are reproduced.

Obstruction of the Nasopharynx Secondary to Choanal Polyp of Antral Origin. Report of Three Cases David Myers Arch Otolaryng 44 328-333 September 1946

Three cases of choanal polyp presenting similar clinical and roentgenologic findings were encountered in a three year period during which over twenty five thousand otorhinologic examinations were made. The diagnosis is based on a history of severe chronic nasal obstruction a profuse purulent nasal discharge usually times a feeling of obstruction in one or both ears with gradual impairment of hearing. Examination reveals a large polyp most frequently single which projects from the middle meatus completely filling the nasal chamber and extending into the nasal pharynx. Posterior rhinoscopy reveals a large mass in the nasopharynx. The mass is easily felt with the palpating finger. Postero anterior roentgenograms of the sinuses show evidence of chronic inflammation in the antra and in lateral views a large globular mass extending into the nasopharynx is seen. Pathologically this growth resembles a nasal polyp and it is usually so diagnosed. It differs from a nasal polyp however in that it is firmer

and contains a great amount of dense fibrous connective tissue which may be undergoing myxomatous changes. The treatment of choice is the Caldwell Luc operation with removal of both the nasal and antral portions of the polyp.

Mandibular Tumors A Clinical, Roentgenographic, and Histopathologic Study Louis T Byars and Bernard G Sarnat Surg Gynec & Obst 83 355-363 September 1946

The object of this paper is to demonstrate (1) that many mandibular tumors may roentgenographically resemble ameloblastomas and (2) that ameloblastomas do not have a constant characteristic roentgenographic picture. These observations are tersely exemplified by a series of 12 brief case reports with reproductions of roentgenograms and photomicrographs. Multilocular radiolucent areas in the mandible are demonstrated in ameloblastoma multiple follicular cyst giant cell tumor fibroma fibrosarcoma osteogenic sarcoma, and metastatic carcinoma from breast and thyroid. A concise table is given of the characteristics of mandibular tumors which appear multilocular on the roentgenogram. It is emphasized that the histopathologic diagnosis is specific. The roentgenographic diagnosis, however is non-specific and includes many tumors which though radiolucent are not truly cystic. For this reason a roentgenographic classification is given dividing tumors into those of dental and non-dental origin.

The authors emphasize that the diagnosis of ameloblastoma or any other tumor of the mandible should not be made by the roentgenogram alone. The prime value of the latter is to show the site and extent of these multilocular lesions.

ARTHUR W PRYDE M D

Radiologic Investigation and Diagnosis of Laryngeal Fractures R Mathey Cornat and Pellegrino J de radiol et d électrol 27 419-422 1946

Case histories are given to illustrate the manner in which radiologic examination may supplement direct examination to clarify diagnosis in laryngeal fractures. In one case a lateral view demonstrated a fracture of the right greater cornu of the thyroid cartilage. In another the alae right and left had been fractured. The most informative projections were the two lateral views plain and with a Valsalva effort. Subcutaneous emphysema is usually noted. Edema of the larynx is an important complication as is hematoma formation. Tomography when available may be of great aid.

PERCY J DELANO M D

Laryngocoele Mac D Campbell Arch Otolaryng 44 219-222 August 1946

Laryngocoeles have been divided into three classes (1) internal a cystic dilatation within the larynx of the ventricle of Morgagni that penetrates the thyroid membrane just above the upper rim of the thyroid cartilage and anterior to the superior cornu or just lateral to the thyroid notch. (2) a combination of (1) and (2). A case of the second type is reported. A 33-year old soldier had a visible tumor which rose with swallowing in the anterior superior triangle of the left cervical region. It was soft and compressible and could be collapsed with a squealing sound when the patient's mouth was open. Indirect and direct laryn-

bones were thick and well marked digital impressions were seen in them. Encephalographic studies showed normal filling of the cisterna magna the fourth ventricle and the aqueduct, but no filling of the third ventricle and the lateral ventricles. Additional air merely outlined the other basilar cisterns and the cerebral sulci which appeared normal. Treatment with pheobarbital and Dilantin[®] abolished the epileptic manifestations and improved the temperament of the child.

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survey should be undertaken until there has been adequate planning for each step in the process

One of the first steps is the notification of the negative group, which he believes should include such minor findings as abnormal ribs slight pleural thickening and calcifications For this he recommends the notification form used by the U S Public Health Service, reading

"On the date shown below, an x-ray was taken of your chest You will be glad to know that the condition of your lungs appears satisfactory on this x-ray film" About 95 per cent of the group surveyed will receive such notification Contact with the positive group may be by letter or by the public health nurse One voluntary organization found that 40 per cent of those approached only by letter responded and were re examined, but that this figure rose to 63 per cent when a visit from the public health nurse was added

A special plea is made for protection of the patient's economic interests and for the maintenance of the private practitioner patient relationship

MAURICE D SACHS, M D

Pulmonary Cavitation, Difficulty in Differential Diagnosis by X-Ray Norman Diamond Dis of Chest 12 422-430, September-October 1946

Cavitation in the lung, with whatever disease it is associated, represents an identical pathological process, namely, destruction of the parenchyma with resultant interruption of the pulmonary framework The excavations assume a given shape or appearance as a result of elastic retraction of surrounding lung tissue, partial bronchial occlusion, and marginal atelectasis of the surrounding alveoli The roentgenographic appearance of a cavity, with or without a fluid level is nothing more than a high light The identification of the specific etiology of the destructive lesion becomes then a clinical problem, to require the roentgenologist to give a precise diagnosis without a clinical work up is to place him in an unfair position While the author believes that in the final diagnosis most of the emphasis should be placed on the clinical aspects, this does not minimize the value of the roentgen study for it is admitted that most cavities would be missed if left solely to clinical and physical examination

A table is presented listing diseases with cavitations and their characteristics, and roentgenograms are reproduced to show the similarity of the appearances in examples due to different causes

HENRY K TAYLOR M D

Appearance of Reinfection Tuberculosis in Children. José Rodríguez Betancourt Miguel A Valiente Carlos Amador and Pedro G Hoyos Bol Soc cubana de pediat 17 131-146 April 1945

The most frequent type of reinfection tuberculosis in childhood is the so-called secondary or post primary infiltration, due to a reactivation of residual foci of disease Among 2100 cases of active tuberculosis in children studied by the authors about 300 (14 per cent) were of this type, while only 41 examples (2 per cent) of tertiary infiltrates were observed The clinical picture varies, ranging from complete absence of symptoms to an acute condition with fever and signs of consolidation Hemoptysis was never observed by the authors in this group

The peripheral region is the usual site of the secondary lesions though there may be involvement of other parts of the lungs especially the bases The infiltrate may

assume a triangular form or may appear as a transverse band or a mass invading one or more lobules The appearance is homogeneous

The usual course is benign, with healing in one or two years Relapses occurred in some of the authors' cases but in these, too, healing eventually followed In some few cases caseation ensues, with eventual cavitation Under such conditions the symptomatology is obvious, the shadow lacks homogeneity, and the patient grows progressively weaker Other manifestations of the secondary process may appear at the same time as the pulmonary lesions, pleurisy, peripheral adenopathy, phlyctenular conjunctivitis, tuberculous peritonitis, etc

The tertiary type of the disease, seen in older patients, represents a new focus, in a previously sound lung or at the site of an earlier lesion Since the clinical picture is not always clearly defined, radiologic examination and other auxiliary methods of diagnosis are of special importance About a third of the cases are of acute onset with high fever and respiratory symptoms The infraclavicular region is the usual site of the lesion in the beginning Radiologically it appears as a rounded or oval shadow, about 2 cm in diameter, of moderate density, more intense at the borders Caseation cavitation, and dissemination are of frequent occurrence On the other hand, healing may take place or the disease may remain stationary for a considerable time There may or may not be an associated osteo-articular tuberculosis

The differential diagnosis between early infiltrations and secondary infiltrations is difficult if the patient's history is unknown or there has been no previous tuberculin test Sometimes films will show traces of the early infection surrounded by the secondary infiltration, but it is frequently impossible to determine whether one is dealing with a late primary infection or an early secondary one Differentiation of the tertiary infiltration is in general easier The greater age of the patient, history of exposure and of an earlier positive tuberculin test the site of the lesion, the calcified primary complex, the rapid evolution toward caseation with demonstration of the tubercle bacillus in the sputum are factors of great value Even in these cases, however, differentiation is sometimes impossible and the true condition is revealed only at necropsy VICTOR GIANNONI M D

Sarcoidosis—A Manifestation of Tuberculosis Charles Cameron and E K Dawson Edinburgh M J 53 465-484, September 1946

A case of pulmonary tuberculosis with pathological changes in other tissues conforming to the accepted clinical and histologic features of sarcoidosis is reported The history is given in detail and covers a period of almost fifteen years—from the time of the initial disturbance, when the patient was five years old until her death at nineteen and a half A diagnosis of pulmonary tuberculosis was first made at eight years of age though an increased hilar shadow had been present three years earlier, when the patient first came under observation for a rheumatic condition After the age of eight she had a persistent cough, and by fourteen years the lung picture suggested a chronic fibrotic type of tuberculosis The roentgen appearance was that of a chronic fibrotic tuberculous lesion of the right upper lobe, with diffuse abnormal shadows in both lungs of the sarcoidosis type Such shadows resemble closely those of chronic miliary tuberculosis especially

gastroscopy revealed nothing abnormal. Anteroposterior and lateral views of the cervical spine showed a cyst-like tumor, approximately $6 \times 4 \times 4$ cm, on the left side of the neck at the level of the hyoid bone. The "tumor" was filled with air and displaced the larynx to the right. Fluoroscopy of the upper part of the esophagus after oral administration of barium failed to reveal any communication between that part of the esophagus and the tumor. At operation a diverticulum of the larynx with active chronic mural inflammation was found.

THE CHEST

Aplasia of the Lung W M Pierson *Ann Otol, Rhin & Laryng* 55 604-608, September 1946

The diagnosis of true aplasia of the lung by roentgen examination, bronchoscopy, and bronchography in an infant of eight months appears to be sufficiently rare to justify publication. The child was first seen at the age of five months with slight dyspnea developing during the course of a head cold. X-ray examination showed a dense shadow in the lower portion of the right chest. The mediastinal structures were displaced far to the right. The cardiac shadow and the right diaphragm could not be identified. Barium was given by mouth and the esophagus was shown to be in the right chest. All the films showed air in the upper right chest which was attributed to hypertrophied lung tissue on the left side which had crossed over to the right side.

Bronchoscopy the following month revealed no evidence of a carina or a right bronchus. Two months later bronchography was done following the introduction of iodized oil through a tracheal catheter. The trachea was well outlined by oil and was seen to continue downward into what appeared to be the left main stem bronchus which also filled with oil. No bifurcation of the trachea was demonstrable. The obvious diagnosis was absence of the right main bronchus and lung.

Absence of a lung does not necessarily forecast an early death as cases have been reported in patients aged 58, 65 and 72 years all of whom died of causes unrelated to the anomaly. Symptoms in many cases are absent, the condition being discovered only by accident. Dyspnea, cyanosis and a failure to thrive may be noted in the very young. The external symmetry of the thorax is maintained in most cases. The heart and the mediastinal contents are displaced to the affected side and the apical impulse of the heart is pronounced. Dullness or flatness on the affected side is common. Resonance may be present due to the hypertrophy and emphysema of the remaining lung. Breath sounds may be absent or suppressed. The usual roentgen interpretation is massive or fetal atelectasis.

STEPHEN N TAGER M D

Agenesis of the Right Lung with Death Following Aspiration of Foreign Bodies into the Left Lung Horace E Mitchell *Ann Otol, Rhin & Laryng* 55 609-616 September 1946

It seems probable that a total of more than 80 possibly nearly 100, cases of agenesis of one lung have been reported in the literature. At least one case of absence of both lungs has been observed (Gruenfeld and Gray *Arch Path* 31 392 1941). A paralysis of the diaphragm on one side and diaphragmatic hernia may

present similar clinical and roentgen findings but tomography, bronchoscopy and roentgenologic study following introduction of lipiodol into the tracheo-bronchial tree should yield sufficient information to make a correct diagnosis. Bronchoscopy is the most important feature of a complete examination. The bronchoscopic findings vary. In some cases there is a bronchus or rudimentary bronchus on the side on which the lung is absent, in others there is no such rudiment. If a bronchus is present, as a rule no opening can be visualized.

The cause of agenesis of the lung is not definitely known. Disagreement exists among embryologists and anatomists as to whether the defect is present in the original germ plasma or is a result of some disturbance occurring early in the development of the embryo.

The case here reported was published previously as one of a series of cases of foreign bodies in the air and food passages (*Ohio State M J* 32 950 1936). A two-year-old child stumbled and fell aspirating some partially masticated peanuts and chewing gum into the tracheo-bronchial tree. Dyspnea and cyanosis immediately followed and death occurred about twenty minutes later before an examination could be made. At autopsy, the left lung was found to be hypertrophied filling the left side of the chest and extending beyond the mid line. The right lung was completely absent with the bronchus ending blindly. A section through the stump showed nothing but cartilage. No rudimentary right lung tissue nor vessels were found. When the left bronchus was opened two foreign bodies consisting of masticated masses of chewing gum and peanuts were found. STEPHEN N TAGER M D

Observations on Mass X-Ray Surveys Waldo R Oechsh *Calif Med* 65 Tuberculosis Supplement pp 29-31 August 1946

Lack of equipment and personnel stands in the way of the realization of the goal of the Public Health Service which is that every person in the United States should have a chest x-ray examination. There is however one method of case finding which can be more readily put into effect that should yield a considerable number of cases, namely the routine examination of all patients entering general hospitals. Protection of hospital personnel should in itself justify such a program. Statistics from one large university have shown that student nurses on a general hospital service have 100 times the chance of acquiring tuberculosis as students in the school of education. The author stresses the importance of the 14×17 inch film for making an actual diagnosis after the miniature film has been studied.

A special warning is issued against the dangers of excessive irradiation of personnel engaged in photofluorographic surveys. Dangers due to technical mis calculations such as too high insertion of the lead glass window in the screen or inadequate lighting over the patient, can be avoided by attention to these details.

MAURICE D SACHS M D

Putting Miniature Films to Work—Follow-up by Health Department. W G Winter *Calif Med* 65 Tuberculosis Supplement pp 31-33 August 1946

The author feels that too great emphasis has been placed upon mass chest x-ray surveys without sufficient consideration of the tuberculous patient's care once he has been discovered. It is strongly felt that no

type The first runs an acute course and is marked by a dense network of strands with little if any evidence of granulation The second is somewhat slower in its evolution, the network is inconspicuous, but milary lesions are much in evidence Transitional forms probably occur If no obvious network is seen, and if there are no increased hilar shadows but disseminated milary lesions are present, a blood spread of secondary carcinoma and not generalized lymphatic carcinomatosis might be suspected BERNARD S KALAYJIAN M D

Primary Atypical Pneumonia A Disease of Segmental Distribution W E Crysler Am J Roentgenol 56 324-336 September 1946

In an earlier paper (Am J Roentgenol 51 280 1944 Abst in Radiology 43 404 1944) the author made the following observations on the roentgenographic findings in atypical pneumonia The process is usually basal but the upper fields are not immune, in the established case, as a rule, the roentgen opacity is homogeneous and translucent, early characteristics are blurring of the structural markings fanwise from the hilum, resolution is almost a complete reversal of these changes intensification of the bronchovascular markings being the last sign to disappear The further generalization is now made that in this form of pneumonia the infiltration is essentially segmental in type, the distribution being closely related to the zones supplied by the secondary rami of the bronchial tree The bronchopulmonary segments of the lungs are illustrated and described Frontal and lateral projections have been found best suited for routine localization The lateral roentgenogram affords visualization of pulmonary fields behind the heart and below the summit of the diaphragm

Atypical pneumonia differs sharply from lobar and lobular types in its bronchopulmonary segmental nature This feature is unique The predilection for the basal areas suggests that the disease results from aspiration of the infective agent to cause a descending bronchogenic infection of the pulmonary parenchyma That the dorsal segments of the upper lobes are not involved by atypical pneumonia is of some diagnostic significance for they are favorite sites of pulmonary tuberculosis Recheck in ten days should be done when the latter diagnosis is suspected

Many illustrative cases are given showing the distribution of atypical pneumonia in the various segments supplied by the secondary rami of the bronchial tree The use of the lateral view in routine study of pulmonary disease is strongly recommended

CLARENCE E WEAVER M D

Primary Atypical Pneumonia A Report of 420 Cases with One Fatality During Twenty-Seven Months at Station Hospital, Camp Rucker, Alabama. Walter C McCoy South M J 39 696-706 September 1946

The author gives a detailed analysis of 420 cases of atypical pneumonia in military personnel with the report of a single fatality Patients were studied in regard to diagnosis on admission symptomatology physical findings laboratory and x ray studies clinical course, complications and treatment

There was no appreciable correlation between the incidence of common respiratory infections and atypical pneumonia during the twenty seven month period covered by the report

Despite the minimal physical findings as compared with x ray evidence of pulmonary involvement daily

examination of the chest during the acute phase of illness showed some physical findings in 94.25 per cent of the cases studied

Only cases with proved x-ray evidence of pneumonia are included in this study In all but 9 cases more than one film was made, most of the cases had two to four films, and in a few six or more were taken Initial films showed all variations from a very slight infiltration to complete consolidation of an entire lobe, often with secondary infiltration of another lobe Atelectatic changes were frequently encountered and often residual horizontal thickenings interpreted as 'atelectatic plates' by the roentgenologist, were noted for as long as six to eight weeks after the first chest film It was the author's policy to discharge no patient until the lungs were entirely clear on physical examination and completely cleared—or with only few slight residual changes—roentgenographically In patients who were afebrile for two weeks, with normal blood studies persistent slightly thickened markings or thin atelectatic plates were not considered a contraindication to full duty

The most striking complication in the entire series was the tendency toward involvement of more than one lobe, which was noted in 41 cases (9.7 per cent) The lobes most commonly involved were the lower ones either singly or in combination followed in order by the right upper, the right middle, and the left upper lobe There were all types of combinations including both upper lobes, the entire right lung (2 cases), and the entire left lung (1 case) The most extensive involvement noted was in the one fatal case in which all lobes except the left upper were involved In one case infiltration was limited to the azygos lobe

In the majority of cases the lungs had cleared both clinically and roentgenographically within three weeks In 13 instances clearing required more than five weeks Complications usually mild in this group included extension of the pneumonic process, pleural involvement and delayed resolution

The treatment of atypical pneumonia is symptomatic Sulfonamides are valueless In the more severely ill patients oxygen and transfusions are helpful In the treatment of complicated cases penicillin deserves further evaluation BERT H MALONE M D

Miliary Pneumonia of a Peculiarly Severe Course (Miliary Virus Pneumonia) W Löffler and S Moeschlin Schweiz med Wchnschr 76 815-818 Sept 7 1946

The author describes a new clinical form of virus pneumonia which he terms miliary virus pneumonia It is characterized by a severe often fatal course deep cyanosis and dyspnea, with a lung picture of miliary to nodular infiltration Seven case histories are presented

The onset was usually acute with a more or less non-specific prodromal stage In 3 of 4 cases studied the blood showed typical cold agglutinins The picture can be mistaken for a miliary tuberculosis In the 4 fatal cases necropsy showed a miliary bronchopneumonia with bronchiolitis obliterans The therapy employed was intensive use of sulfonamides and penicillin The importance of the condition lies in its differentiation from the roentgenologically similar miliary tuberculosis and in the fact that the cold agglutinins may agglutinate the red cells at room temperature leading to false blood grouping reactions

LEWIS G JACOBS M D

of the lymphogenous type and the differentiation of the two conditions is often a matter of personal opinion. Skin lesions resembling bruises, appeared on the lower limbs at the age of nine. Their histologic nature was not determined at that time. When the patient was fourteen both eyes became involved by an iridocyclitis and at the same time a profuse culture of tubercle bacilli was obtained from the sputum. Shortly afterwards hematuria occurred and during the next year the liver became enlarged. Swelling of the joints first observed at the age of six, remained unchanged and there was a persistent albuminuria. At the age of sixteen and a half the patient had an attack of right renal pain associated with pyuria. Two months later a skin rash appeared. Tubercle bacilli were again found in culture this time from gastric lavage. The nature of the skin condition sarcoid in distribution (mainly limited to face and limbs), was now confirmed histologically. In addition to these localized foci of disease there was also a systemic disturbance, manifest in underdevelopment in size and weight and the absence of secondary sexual changes. A congenital cardiac condition apparently unrelated to the other lesions may have been responsible for the failure of development. The patient died a cardiac death following influenza and bronchopneumonia. Autopsy or biopsy of a joint was not permitted.

The relationship of tuberculosis and sarcoidosis is discussed at length.

Bronchiectasis Following Primary Tuberculosis

Edna M. Jones, W. M. Peck and H. S. Willis. *Am J Dis Child* 72: 296-309, September 1946.

In a study of 716 children with pulmonary tuberculosis by Jones, Rafferty and Willis (*Am Rev Tuberc* 46: 392-1942) 85 showed in roentgenograms a dense more or less homogeneous and usually segmental or lobar shadow that suggested obstructive pneumonitis. 42 of these were examined bronchoscopically and 31 were found to have tuberculous involvement of a bronchus in the form of ulceration, granulation tissue, tuberculoma or extrinsic pressure from enlarged nodes. Several years later some of these children together with others showing the same phenomenon were studied by bronchography.

The authors obtained satisfactory bronchograms in 34 of the 37 children examined and demonstrated bronchiectasis in the area of former pneumonitis in 24 children but no bronchiectasis in 10. They used the catheter method of direct instillation of iodized poppy seed oil. Only the involved side was studied. Bronchiectasis was found in only 4 patients who had had their pulmonary lesions twelve months or less. The other 20 had been ill thirteen months or longer. The bronchography was done at a mean interval of three and a half years after roentgen clearing of the original lesion. It was concluded from these observations that the duration of the disease was important and that the damage was permanent. There was a preference for localization of the bronchiectasis in the anterolateral branch of the upper lobe bronchus and in the apical branch of the lower lobe bronchus.

These children had symptoms representing both the primary complex and obstruction and the bronchiectasis. There were few symptoms referable to clinical bronchiectasis after the clearing of the pneumonitis and tuberculosis.

Treatment suggested includes steam inhalation to

thin the secretions, the judicious use of theophylline, ethylenediamine, and postural drainage. When a tuberculoma, granulation tissue or ulcer is present bronchoscopic treatment is indicated.

PAUL W. ROMAN, M.D.

Generalized Lymphatic Carcinomatosis (Cancerous Lymphangitis) of the Lungs, with Special Reference to Miliary Carcinomatosis and the Syndrome of "Granule Froide"

C. G. Lambie and J. Collier. *M. J. Australia* 2: 439-446, Sept. 28, 1946.

The presence of miliary infiltrations widely disseminated throughout the lungs but unaccompanied by the clinical evidences of miliary tuberculosis has produced the term 'granuloma froide' among French physicians. The existence of subacute or chronic miliary tuberculosis has been questioned by many physicians. A similar appearance may be produced by sarcoidosis, pneumoconiosis, mycotic disease of the lungs, lymphogranulomatosis and other etiologic agents. The author presents the details of a case in which the picture was due to a miliary carcinomatosis.

A 34-year old woman had had repeated attacks of cold and influenza with a dry cough and pain in the back over the lower ribs. The cough and pain increased in severity, the sputum became more abundant, hemoptysis occurred and there were progressive anemia, weakness, loss of weight and finally respiratory embarrassment. Repeated tests showed no evidence of tuberculosis and none of the usual clinical signs of sarcoidosis was present. Bronchoscopic examination showed multiple small nodules on the mucous membrane of the trachea and left bronchus and a marked narrowing of the right bronchus for about one inch just below the origin of the upper lobe bronchus. No material could be obtained for biopsy. The narrowed area was hard, granular, irregular and bled easily.

The radiographic appearance was believed to be characteristic of miliary tuberculosis though the infiltrations were somewhat coarser than those ordinarily seen in that disease. Later some confluence of the shadows occurred in the right lower lobe area and still later there developed evidence of pleural effusion on the right. Films of the spine showed erosion and anterior wedging of the eleventh dorsal vertebra which increased during the course of the disease.

At autopsy an extremely widespread miliary carcinomatosis was found in the lungs with the densest lesion in the right lower lobe and metastases in the ascending colon, the right ovary, the left kidney, the eleventh thoracic vertebral body, the left sixth rib and the liver. The exact primary site was not determined although the histology would indicate that it was probably bronchiogenic.

Acute miliary carcinomatosis usually runs a rapid course—seldom over two months from the appearance of the first symptoms. In this case the duration of the symptoms was over one year but the course was rapidly downhill during the last four months. This is interpreted as indicating that the condition began as a bronchiogenic carcinoma of the slow growing type which suddenly erupted with secondary foci in the mediastinal nodes. This led to invasion of the lymphatics of both lungs with disseminated lesions in all lung fields and an aggravation of the symptoms.

Two main types of generalized lymphatic carcinomatosis of the lungs may be distinguished: a diffuse or non-granular type and a miliary (granular or nodular)

A review of the chest films in these cases of delayed chemical pneumonitis showed that the roentgenologic appearances fall into three distinct stages, not counting the variable latent period (3 months to 3 years) in which the lungs appear normal

Stage 1 The earliest recognizable variation from the normal is a diffuse granularity, presenting a fine sand-paper appearance, which under magnification suggests a sandstorm. There are no increased linear markings, no nodules, no coalescent lesions, no pleural thickening, and no pleural effusion. The appearance is not the smooth homogeneous ground glass appearance of pulmonary edema or consolidation, but distinctly particulate in appearance. It is uniform and diffuse, extending to the periphery and including the apices although at first glance the latter regions seem to be spared. The hilar vascular shadows are usually normal and distinct in this stage.

Stage 2 The second stage is characterized by a diffuse reticular pattern on the granular background. The hilar vascular shadows become fuzzy and indistinct and slightly enlarged. Only three patients showed enlarged hilar nodes, moderate in degree in two instances rather marked in one.

Stage 3 Distinct nodules appear uniformly through the lungs varying from 1 to 5 mm in diameter and the appearance now resembles a snow storm. Several cases in this stage have shown multiple small dark areas between the reticulonodular shadows giving an appearance on a single film resembling the cut surface of a sponge. These could be due to small areas of emphysema. The nodules are evenly distributed throughout both lungs. They do not coalesce, do not calcify or cavitate, and there is no definite linear fibrosis. The hilar shadows are quite fuzzy and indistinct, probably due at least in part to surrounding and overlapping nodulation. Pleural effusions are still absent, but the heart shadows in this stage become slightly larger and the pulmonary artery may be quite prominent. No basal emphysema is demonstrable although one patient's films showed progressive upward displacement of the hila and the interlobar fissure on the right side.

The terminal picture may be complicated by heart failure (pulmonary congestion, hydrothorax and cardiac dilatation), but no films were seen in this stage.

One patient apparently did not go beyond Stage 1, then showed subsequent clearing but did not return to normal, the granular appearance is still recognizable. One other patient improved roentgenologically after reaching Stage 3 (early) the hilar shadows remain enlarged and the lung markings are definitely exaggerated, but the nodularity and the granularity have disappeared.

The roentgen appearance in the third stage may be closely simulated by sarcoidosis or lymphangioectatic carcinomatosis or an occasional case of erythema nodosum with marked pulmonary changes. It is less closely simulated by acute silicosis, miliary tuberculosis, a rare case of diffuse fungus infection and occasionally by the diffuse pneumonitis and miliary atelectasis which may follow an acute virus infection.

The cardiac changes were obviously pre-existent or secondary to the increase in pressure in the pulmonary circulation. One would have expected cyanosis to be reported more constantly. The presence of clubbing in the extremities in only two cases is hard to understand.

Pulmonary Actinomycosis (Report of the First Case Observed in the Isthmus of Panama) Carlos Calero Dis of Chest 12 402-408 September-October 1946

A 12-year-old native white girl first came under observation in December 1944 with a diagnosis of pleuropulmonary fistulae. A year earlier she had sustained severe trauma to the left hemithorax which resulted in hospitalization and subsequent surgical drainage for empyema. Repeated sputum examinations were negative. No improvement followed several courses of sulfa drugs and penicillin. Seven months later the patient was again seen, with three new fistulae. She had lost weight and cough and morning expectoration were worse. The liver and spleen were enlarged, and there were enlarged nodes in the axillary and precervical regions, movable and not tender. Six fistulous openings were observed in the posterior thoracic wall.

A roentgenographic examination of the spine was negative. There were no evidences of an osteomyelitis of any of the ribs. Chest studies made on the original admission revealed a consolidation of the right lower lobe with a tracheobronchial adenopathy. Six months later there was a partial resolution of the lesion in the right base, but pleural thickening on the left side, with an area of consolidation in the left base.

Examination of pus obtained from fistulae revealed the characteristic ray fungus which subsequently was found in the sputum. Following the establishment of the diagnosis the patient was treated with penicillin, thiamine, ascorbic acid, ferrous sulfate, a diet rich in iron and calories, rest in bed, local cleansing and sterile dressings. After seventy-three days she left the hospital apparently cured. She had gained weight, had no cough or expectoration, and the sinus tracts had closed.

HENRY K. TAYLOR, M.D.

Pulmonary Coccidioidomycosis H. E. Bass, S. I. Kooperstein, M. M. Friedman, and G. H. Kastlin Dis of Chest 12 371-383 September-October 1946

Human infection with *Coccidioides immitis* may be seen either as an initial infection (primary pulmonary coccidioidomycosis) or as a disseminated process (coccidioidal granuloma). The latter form apparently represents a lymphohematogenous dissemination of the primary infection to the lymph nodes, skin, bones, brain, lungs, liver, spleen and other organs.

Most of the initial infections are asymptomatic. When symptoms do occur, the onset is abrupt, resembling an acute respiratory infection with chest pain, cough, expectoration, chills, fever, malaise, anorexia, joint pains and headache. Skin eruptions appear in 2 to 5 per cent of the patients, usually in the form of erythema nodosum, one to two weeks after the onset. The diagnosis is based on (1) history of exposure in an endemic area, (2) roentgen findings, (3) recovery of spherules of *Coccidioides immitis* in sputum or gastric contents and confirmation by animal inoculation, (4) a positive skin test, (5) positive serological tests, (6) increased sedimentation rate and (7) eosinophilia.

The early roentgen picture resembles an atypical or bacterial pneumonia. It may be lobular or lobar in extent with single or multiple lesions located at the hilum or at the periphery. Enlarged hilar nodes may be present. Resolution takes place in one to three weeks. A pleural effusion may accompany and obscure the underlying process. During resolution well circumscribed

Q Fever in the Mediterranean Area Report of Its Occurrence in Allied Troops Clinical Features of the Disease Frederick C Robbins and Charles A Ragan Am J Hygiene 44 6-22 July 1946

Epidemics of Q Fever Among Troops Returning from Italy in the Spring of 1945 Clinical Aspects of the Epidemic at Camp Patrick Henry, Virginia. Marcus Feinstein Raymond Yesner and Jerome L Marks Ibid pp 72-87

A Laboratory Outbreak of Q Fever Caused by the Balkan Grippe Strain of Rickettsia burneti Commission on Acute Respiratory Diseases Ibid pp 123-157

The three papers listed above are included in an extensive symposium on Q fever occupying an entire issue of the *American Journal of Hygiene* and covering in great detail the clinical epidemiologic, and etiologic features

Q fever is a rickettsial infection originally reported from Australia (1935) and occurring epidemically and endemically in the Mediterranean area and sporadically in Panama during the latter part of World War II. A significant feature of the disease is pulmonary infiltration demonstrable roentgenographically and a diagnosis of atypical pneumonia has not been uncommon through certain clinical epidemiological and laboratory findings do not wholly correspond with those in the latter disease

Robbins and Ragan in their account of Q fever as it was observed among the troops in Italy describe the roentgen findings as consisting in patchy areas of pneumonic consolidation of homogeneous ground glass appearance usually involving only a small portion of a lobe. Some collapse of lung tissue with shift of the interlobar septum was common. The majority of the cases showed single lesions but occasionally two lobes were involved. There did not appear to be any correlation between the severity of the disease and the degree of pulmonary involvement. The roentgen changes tended to be persistent and of one group of 33 patients who were carefully followed only 6 had negative films on discharge from the hospital (average period of hospitalization for this group 22 days).

The most common clinical features in the Italian outbreak were an abrupt onset with chills, sensations and malaise, high fever of four to fifteen days duration, frontal headache, anorexia, minimal physical signs and fairly rapid convalescence. The diagnosis was established by isolation of the rickettsiae in guinea-pigs and demonstration of the development of specific antibodies in the blood of convalescents by means of complement fixation and agglutination tests.

The epidemic at Camp Patrick Henry, Virginia, reported by Feinstein, Yesner and Marks occurred among troops recently returned from Italy and is considered to be a part of the large Italian epidemic. The outstanding characteristic of the disease as seen here was the roentgen picture and thus the authors describe in detail. To determine the distribution of the lesions they divided each lung into three zones: upper, middle and lower. Lesions were present in the upper zones in approximately 10 per cent of the patients, in the middle zones in approximately 40 per cent and in the lower lung fields in approximately 60 per cent. They were evenly divided between right and left lung fields. Of special interest is the fact that more than 60 per cent of the patients had lesions which involved more than one zone and in 25 per cent of the patients at least 3 or more

zones were involved. This distribution of lesions or at least their multiplicity, is felt to be one of the distinctive findings in Q fever in contrast to cases of primary atypical pneumonia as they are seen in military populations.

The lesions were of three types described as follows: "(a) Bronchitic type which includes lesions at the lung roots, enlargement of perihilar nodes and abnormally increased bronchovascular markings. (b) Peribronchitic type, which includes lesions frequently in the outer two-thirds of the lung fields of the type usually associated with primary atypical pneumonia. (c) Alveolar type, which includes lesions usually in the outer one-third of the lung field that were clearly circumscribed in character and of rather uniform ground glass density with peribronchial markings not being visible in the central portion of the lesion. In addition to the three types of parenchymal infiltration, pleuritic involvement was indicated by thickened pleural shadows and prominent fissures. The majority of the lesions were alveolar or peribroncho-alveolar in character. Evidence of pleural involvement was found in 10 cases.

In the laboratory outbreak described from Fort Bragg 16 cases occurred. Fourteen of the patients exhibited roentgen evidence of pneumonia and in 2 subjects there were also signs of pleural fluid. As in the other series reported, lower lobe involvement predominated. The earliest lesions appeared in the peripheral portions of the lung. They tended to be circular in shape and had the appearance of ground glass. The center of the lesion was denser than the periphery. The lesion increased in size by extension and usually remained circular except where demarcated by the interlobar fissures. The hilar region was singularly free of involvement. The maximum infiltration was usually visualized between the sixth and tenth day of the illness which was about the time that the temperature became normal. In patients with multiple areas of pneumonia, some lesions were regressing while others were developing. The pneumonic process regressed slowly, the involved area clearing in a centripetal fashion.

Delayed Chemical Pneumonitis Occurring in Workers Exposed to Beryllium Compounds. Harriet L. Hardy and Irving R. Tabershaw. J. Indust. Hyg. & Toxicol. 28: 197-211, September 1946.

Seventeen cases of a delayed chemical pneumonitis occurring in employees of a concern manufacturing fluorescent lamps are presented. All 17 workers (3 men, 14 women) were employed in one building during the same period of time. Evidence from the literature suggests that in some unknown manner the fluorescent powders which contain beryllium compounds are of etiologic importance. No other condition or substance which is known to cause pulmonary symptoms had been discovered in the common working environment of these 17 patients. At the time of the report 6 patients had died, 6 were gradually improving though still under medical care, one was completely well, one acutely ill and the other 3 still seriously disabled.

The disease is of unusual interest because of its clinical features—delayed onset, intense dyspnea, weight loss and poor prognosis. In 4 cases symptoms developed while the patients were still at work after a long period of employment in the common environment. In a second group symptoms developed between three and eighteen months after cessation of employment and a third group first complained between two and three years after discontinuing work.

tained (reproduced in the article), recovered because the perforation took place into the pancreas and failed to soil the peritoneal cavity. The high mortality rate in spite of prompt surgical treatment is ascribed to the presence of barium sulfate in the extravasated matter. In addition 3 cases of acute hemorrhage as a result of barium meals are described. LEWIS G JACOBS M D

Peptic Ulcer of the Esophagus Report of a Patient with a Ten Year Follow-up D R Morton and A Brunschwig *Gastroenterology* 7 314-319 September 1946

The authors present a case of peptic ulcer of the esophagus in a 65-year-old woman first seen in 1935 when she complained of vomiting after every meal and a weight loss of forty-five pounds. Roentgen examination suggested a scirrhus carcinoma of the esophagus. A cholecystectomy and a Pezzer catheter gastrostomy were carried out. On three occasions during the next six months, esophagoscopy with biopsy was performed. All three examinations showed a narrowing to 4 mm of the mid portion of the esophagus. All gave the impression of carcinoma but the three biopsies revealed chronic ulceration. Other than having to return every six months for replacement of the Pezzer catheter because of erosion by gastric juice the patient enjoyed excellent health, gained weight and gradually was able to take a pint of milk and one soft-boiled egg by mouth each day. The main part of her nourishment was taken through the gastrostomy catheter. Roentgenography in November 1937 showed almost complete occlusion of the esophageal lumen. The patient was not seen again until November 1945. For the previous five months she had been having intermittent attacks of vomiting. Roentgen studies performed elsewhere were said to show advanced carcinoma of the terminal esophagus and the pylorus. Repeat roentgen examination by the authors revealed no change in the esophageal lesion except less irregularity of the lumen in the constricted segment and a crater 3 mm in diameter in the duodenal bulb. On esophagoscopy the esophagus was found to be normal to within 2 cm of the constricted area. The posterior wall at this point was red. Anteriorly there was a tough rim (fibrous) which narrowed the lumen and prevented passage of the instrument. The No 15 and 20 bougies were passed the former without resistance. The patient was treated with parenteral fluids, vitamins, phenobarbital and tincture of belladonna. Gradually she was placed on milk and cream by gastrostomy catheter and rapidly showed improvement, being discharged in a few weeks in good general condition. It is thought that the active duodenal ulcer might be associated with the presence of the Pezzer catheter in the stomach for ten years.

Perforation of the Esophagus Not Caused by Instrumentation Review of Eight Cases C W Engler *Ann Otol Rhin & Laryng* 55 667-680 September 1946

Perforation of the esophagus is of relatively rare occurrence. It is always a potentially serious condition requiring superior judgment and skill in management. Although cancer is generally cited as the most common cause it was responsible for none of the 8 cases here recorded. Six of these were due to ingested foreign bodies, one to a caustic burn (ingested lye) and one to

syphilis, in the two latter instances a broncho-esophageal fistula was formed.

Of the 6 patients with perforations caused by foreign bodies 2 were treated conservatively and experienced spontaneous recoveries, the other four were subjected to mediastinotomy, with recovery in three and death from a fulminating paraesophageal infection after removal of the foreign body (a denture) in the other. Both patients with broncho-esophageal fistula died the first by suicide after discharge from the hospital and the other from the disease.

In all cases, roentgenographic examinations and endoscopy were important in establishing the diagnosis. Characteristic roentgen changes have been listed (McGibbon and Mather *Lancet* 2 593 1935) as follows: (1) a bubble of air or gas surrounding the point of a perforating foreign body in the cervical region; (2) forward or lateral displacement of the esophagus; (3) increase in depth of the space between the bodies of the cervical vertebrae and the trachea; (4) widening of the mediastinal shadow in the anteroposterior view; (5) passage of barium from the esophagus into the tracheobronchial system; (6) opaque medium outside the esophagus. All these findings were clearly demonstrated in this series. STEPHEN N TAGER M D

Peptic Ulcer A Roentgenological, Laboratory, and Clinical Follow-up of 200 Peptic Ulcers A J Delario *Am J Digest Dis* 13 260-270 August 1946

The incidence of peptic ulcer varies greatly in various countries. Climate, occupation, food habits and hereditary influences may all be causative factors. It is well known that individuals inherit certain tendencies or weaknesses which under stress will make themselves manifest. The weakness commonly encountered in peptic ulcer patients is usually associated with the hyposthenic type of body. The low-lying stomach empties poorly and allows for accumulation of gastric contents and its position may inhibit proper blood supply. These factors may be precursors of peptic ulcers.

A thorough study of 200 peptic ulcers (in 185 patients) was made by the author. In this series 19 were gastric, 156 duodenal, 14 parapyloric and 11 gastrojejunal. The patients represented 16 races, of which the Irish were first with 43 cases, the Italian and English second and third with 35 and 34 cases, respectively. There were 5 males to 1 female. A high percentage of the patients (76.2 per cent) were of the hyposthenic type. The age varied from ten to seventy, but the condition occurred most commonly between the twentieth and fiftieth year. There was an increase in the hydrochloric acid content of the stomach in almost all cases, the acidity decreasing as the ulcer improved.

There are two theories as to the cause of pain in peptic ulcer. The first is that the increase in hydrochloric acid irritates the nerves in the ulcer. The second theory is that pain is produced by the increased tonicity and hyperperistalsis of the stomach. Against the theory of increased hydrochloric acid as the cause of pain the author cites the fact that the 9 patients with subacidity in his series had as much pain as those with hyperacidity. That administration of hydrochloric acid by mouth sometimes relieved pain and that experimentally one can apply hydrochloric acid direct to the ulcer without producing pain. He believes that a patient will have pain from an ulcer only when its base is attached to the muscle or submucosa.

scribed nodular densities may appear which ultimately may break down and form cavities

Resolution may be complete and leave no traces in the roentgenogram, or healing may terminate with fibrosis. Serial roentgen studies have revealed the progressive changes with resolution as follows: the initial parenchymal lesion enlarged hilar lymph nodes, nodular lesions excavation, and complete healing with or without fibrotic changes. Residual nodular lesions may persist for months or years. During the resolution phase the lesion may have a honeycomb appearance. Sometimes calcification occurs. The initial pneumonitis of primary pulmonary coccidioidomycosis may be difficult to distinguish from primary tuberculosis, especially when accompanied by hilar adenopathy.

The pulmonary appearance of the disseminated form may resemble carcinoma of the lung, other fungus infections, sarcoidosis, or military tuberculosis.

HENRY K. TAYLOR, M D

Löffler's Syndrome Associated with Creeping Eruption (Cutaneous Helminthiasis). Report of Twenty-Six Cases. D O Wright and Edwin M Gold. Arch Int Med 78 303-312 September 1946

The authors recently (J A M A 128 1082 1945 Abst in Radiology 46 614, 1946) reported 9 cases in which Löffler's syndrome complicated creeping eruption (cutaneous helminthiasis). They now present 17 more cases in which the two conditions were associated making a total of 26 cases of Löffler's syndrome among 76 cases of creeping eruption. This series is reported (1) to establish creeping eruption as an additional etiologic factor in the production of so-called Löffler's syndrome, (2) to prove that creeping eruption is not always a localized cutaneous disease, and (3) to forge an additional link in the chain of circumstantial evidence that Löffler's syndrome is allergic in origin.

Nontraumatic Spontaneous Pneumothorax Among Military Personnel. Samuel Cohen and J Murray Kinsman. New England J Med 235 461-467 Sept 26 1946

This is a report of 39 cases of non-traumatic spontaneous pneumothorax developing during military service. The complaints of these patients were chiefly shortness of breath (more subjective than objective) and pain in the chest radiating to the shoulder, neck, or abdomen. In a lesser number of patients cough, cyanosis, and fever were noted. In 59 per cent of the series the condition occurred while the patient was at rest, in 26 per cent during mild exertion, and in 13 per cent during active physical exertion.

Roentgen study revealed the pneumothorax more adequately than any other type of examination; the best demonstration was in forced expiration. Active pulmonary tuberculosis was seen in 2 patients who were therefore excluded from this study. Inactive tuberculosis of a minimal degree was found in 3 cases or 8 per cent; pulmonary calcifications were seen in 10 per cent. No pulmonary process could be demonstrated in the remaining 77 per cent. The collapse was considered mild in 51 per cent of the patients, moderate in 26 per cent, and severe in 23 per cent.

In considering the etiology of spontaneous pneumothorax, tuberculosis must be considered first. The tearing of adhesions is given as a second cause. A general cystic disease of the lung may cause air to flow

into the pleural cavity as may also rupture of subpleural emphysematous blebs or rupture of an interstitial emphysematous bleb.

The treatment of these patients is considered and their military disposition discussed.

JOHN B McANENY, M D

Case of Spontaneous Pneumothorax in the Newborn. Angelberto de los Heros, Gustavo Cardelle and Reinaldo Martin Jiménez. Bol Soc cubana de pediat 17 185-193, May 1945

The authors present a case of spontaneous pneumothorax in a newborn infant presumably due to rough attempts at resuscitation and stress the danger of such maneuvers by persons of little experience. Radiologic studies in all cases of dyspnea and cyanosis in the newborn are recommended as the best method of reaching a diagnosis.

VICTOR GIANNONI, M D

Spontaneous Hemopneumothorax. A Case Report. Ray Vander Meer. Am Rev Tuberc 54 283-286 September 1946

The author reports a case of spontaneous hemopneumothorax occurring suddenly in a 26-year-old soldier. The patient gave a history of severe left chest pain, marked dyspnea, and cyanosis developing while he was filling in a slit trench. Within twenty minutes he appeared to be in shock but responded well to intravenous fluids, oxygen, and morphine. A chest roentgenogram revealed fluid and pneumothorax in the left pleural cavity and diagnostic thoracentesis on the ninth day yielded pure blood which failed to clot. All blood appeared to have been absorbed by the twenty-fifth day and recovery was uneventful. Approximately 60 cases of spontaneous hemopneumothorax have been reported since 1900. Most authors agree that the bloody fluid obtained on aspiration will not clot. The reason for this is not clear. Conservative treatment is advised.

L W PAUL, M D

Secondary Heart Tumor Diagnosed at Operation. Lorenzo H Martiarena. Rev argent de cardiología 12 13-25 March-April 1945

A case of secondary heart tumor with clinical signs of cardiac involvement diagnosed as a constrictive pericarditis is reported. Roentgen examination of the chest did not show parenchymatous alterations. At operation, however, a tumor of bronchial origin was found hidden by a shadow of right pleural effusion, with strong adhesions between lung and diaphragm preventing the liberation of the heart. Postmortem study revealed a tumor of the right lung which had invaded the right auricle and part of the left. The diagnosis was carcinoma of bronchial origin.

THE DIGESTIVE SYSTEM

Danger Moments (Perforation, Hemorrhage) in the Roentgen Examination of the Digestive Tract. Jean Marc Strasser. Schweiz med Wchnschr 76 705-708 Aug 3 1946

The author reports 7 cases of acute perforation of the stomach or bowel occurring in association with and presumably as a result of barium examination. Five of the patients died with a generalized peritonitis; one patient recovered in spite of peritonitis; and one in whom an actual film record of the perforation was ob-

placed folds of hypertrophic mucous membrane resembling the convolutions of the brain

The polyps are described as either neoplastic or hyperplastic, though it is frequently difficult to distinguish the two types grossly. The congenital neoplastic polyps are usually pedunculated, but may be sessile. They are freely movable on the submucosa and are separated from each other by an area of normal mucosa. The mucous membrane away from the polyps may be normal or show atrophic gastritis. The connective tissue from the submucosa forms a central fibrous tissue core in these polyps. The hyperplastic polyps have defective margins which merge with the normal mucosa. Their edges rise to a hilly slope, and they are flatter and more expansive than the other type. They are firm and immovable on the submucosa which is seen to take no part in the growth as a connective tissue core. The neighboring mucosa shows definite signs of chronic inflammation.

Although gastric polyposis is essentially a benign condition, it is potentially malignant. The frequency of malignant change has been variously reported as from 5 to 40 per cent, 12 per cent is perhaps the most generally accepted figure.

There is no characteristic clinical picture for gastric polyposis. The condition may remain asymptomatic throughout life, or digestive symptoms of varying degree and duration may be present. Laboratory examinations show a high percentage of achlorhydria, absence of ordinary digestive secretions and increased mucus. Blood findings may reveal a secondary anemia or occasionally a picture resembling that of pernicious anemia.

The differential diagnosis roentgenologically between polyps and gastric carcinoma is frequently difficult. The use of a viscid opaque medium given in small quantities may be of considerable help during fluoroscopy. The author recommends the use of films made with compression over the stomach. The polyps usually are more common on the greater curvature side of the lower third of the stomach, where they produce ragged indentations in the barium shadow, resembling mottled, fingerprint filling defects. Gastroscopic study should supplement roentgen study in all suspicious cases.

Radiation therapy for gastric polyps has not proved very successful. Gastric resection is definitely better than attempts at local excision of the polyps, and is the treatment of choice since it eliminates the possibility of malignant change. BERNARD S. KALAJIAN, M.D.

Induced Gastric Hyperkinesia. A New Technique for the Complementary Study of the Stomach and Duodenal Bulb. P. Porcher. *J. de radiol. et d'électrol.* 27: 393-401, 1946.

The author's technique for study of the stomach and duodenal bulb consists in the administration of 1 g of morphine (about 1/6 gr.) ten minutes before administration of the barium meal. This induces a hypermotility of the stomach which has made it possible to uncover many ulcer niches that have eluded discovery on a routine examination.

The illustrations appended are not too convincing, many of those with the stomach exhibiting physiologic behavior appear to the abstractor to give more information than the films made after such vigorous peristalsis had been induced. I believe that many radiologists rely upon pylorospasm and a certain protracted conformation of the pylorus that may go

with it for a preliminary impression of peptic ulcer, a static pylorus may accompany some conditions. Drugs which alter such appearances sometimes rob us of essential information, they become unnecessary if the patient is recalled after a time for further observation.

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PERCY J. DELANO, M.D.

Roentgenologic Studies on the Effect of Synthetic Folic Acid on the Gastro-Intestinal Tract of Patients with Tropical Sprue. R. L. Hernandez Beguerie and Tom D. Spies. *Am. J. Roentgenol.* 56: 337-342, September 1946.

A normal subject and three patients with tropical sprue were used for this study. One of the patients with sprue served as a positive control and received no specific therapy, the others were treated with folic acid. After a barium meal consisting of 100 gm. of barium sulfate in 150 c.c. of water, films were taken at fifteen minutes, forty five minutes, one hour, and each hour thereafter until the head of the barium column reached the cecum.

Synthetic folic acid in daily doses of 10 mg. was found to have a profound effect on the alimentary-tract function of patients with tropical sprue in relapse. The treated cases showed striking improvement which was evidenced by return of intestinal motility toward normal and the establishment of a continuous column of barium which was not interrupted by segmentation or fragmentation. The untreated patient showed no improvement within a similar period of time.

The roentgenographic findings most often observed in this series of patients with tropical sprue were mucosal edema of the small bowel, segmentation with alternating intestinal spasm, and dilatation and hypomotility of the small intestine. These abnormal small bowel patterns may also result from a nutritional disorder, hypoproteinemia, disease of the liver, disease of the mesentery, or any disease condition which produces submucosal edema. CLARENCE E. WEAVER, M.D.

Derangement of Midgut Rotation Producing Volvulus. Report of Two Cases. C. E. P. Markby. *Brit. J. Surg.* 34: 80-83, July 1946.

Two cases of volvulus of the midgut are recorded, one implicating the pre-arterial segment, due to non-rotation, and one involving the postarterial segment, due to an inverse rotation.

The first patient was a girl 7 1/2 years old with a history of constipation and vomiting from birth to the age of 5, at which time she presented symptoms of acute obstruction, relieved by lavage and enemata. She then remained well for one year after which vomiting attacks recurred. On admission, the child's general condition was poor with severe dehydration. Some 30 ounces of clear greenish bile stained fluid were vomited daily. Roentgenoscopic examination in the erect position revealed three fluid levels before any opaque meal was swallowed. These were found to be in the dilated stomach and duodenal cap and in the region of the duodenojejunal flexure. After the barium meal, the second and third parts of the duodenum suggested

Seventy-two operations were performed on the 185 patients. 51 were done because of the ulcer. 21 were listed as miscellaneous and of this latter group 11 were appendectomies.

After years of treatment 20 of the 185 patients even though they showed deformed cups were found not to have duodenal ulcers. The chief cause of missed diagnosis was peritoneal adhesions (6 cases). Chronic cholecystitis was responsible for the deformity in 1 case.

There were only 5 patients who did not complain of pain. Those that had pain waited an average of eight and a half years after the prodromal symptoms were noted before having x-ray examination.

The length of time it took for an ulcer to heal under constant treatment of one type or another averaged sixteen months. The shortest time was two months. The longest time was forty months.

No matter how long the ulcer has existed the fact that the patient has been adequately treated reduces the chance of perforation or the necessity of surgery. 28 per cent of those who were laparotomically treated showed perforation, died or required surgery whereas only 27 per cent of those adequately treated met with these incidents.

There were 14 gastric ulcers in the series, 9 of which were associated with duodenal ulcers. Gastric ulcers as a rule could be cured in from four to eight weeks. The author does not believe that surgery should be employed in the treatment of gastric ulcer. He cites 77 cases followed by Brown to prove that they do not become carcinomatous. Only one of Brown's patients died of carcinoma and this was in the third year of an ulcer.

There were 15 perforations in the series with 14 deaths. One patient lived without operation. The author believes the method of suturing a perforation is wrong. In the hasty effort to save the patient's life the edges of the ulcer are sutured; this restricts the ulcer. The ulcer edges should always be excised if possible.

Obstruction is not an indication for surgery. Just as many patients with obstructions are cured as with out. Under proper treatment the spasm disappears and the stomach can empty itself in six hours even though a lot of scarring exists.

There were 22 hemorrhages reported in this group of cases. It is the impression of the author that they should be treated conservatively. The only cases that should be treated by surgery are those that may not improve because of underlying causes such as arterio-sclerosis or syphilis.

The injection treatment is condemned by the author who believes that any benefit at all derived by the treatment is due to associated dietary measures.

JOSEPH T. DANZER, M.D.

Dyspepsia, Ulcer and Gastric Cancer. T. J. Anglem. *New England J. Med.* 235: 322-325, Sept. 5, 1946.

The author points out that early in the present century Graham Moynihan and others commented upon the long history of gastric distress in many patients who ultimately died of cancer of the stomach. Gastric complaints must not be taken lightly. They should be investigated repeatedly if necessary. In many instances the early history of gastric cancer is typical of benign ulcer; sometimes it is only suggestive of ulcer.

The present study is based on 192 private cases

35 were inoperable. 60 were found to be inoperable on exploration. 18 were suitable for palliative procedures. 20 were suitable for palliative resection. 4 refused operation and 57 were resectable for cure. The average delay before the patient sought medical advice was nine months and before the diagnosis was established there was a delay of seventeen months.

The early symptoms presented by the patients were epigastric pain or burning, distress or fullness. In 17 per cent a history typical of ulcer was present and in 27 per cent a history suggestive of ulcer was obtained.

It is believed that there is a 25 per cent error in the ability of roentgenologists to determine cancer of the stomach. There seems to be an irreducible error of about 10 per cent in the differential diagnosis of gastric ulcer and gastric cancer.

Recent reports show a mortality of less than 5 per cent in gastric resections, all by very competent surgeons. The present author believes resection for gastric lesions is the procedure of choice in view of the low mortality rate and the great possibility of many apparently benign lesions being actually malignant.

A plea is made for earlier diagnosis, closer supervision, and early operation in patients in middle life who complain of gastric distress. JOHN B. McANENY, M.D.

Gastroscopy and Its Relationship to Roentgenology in the Diagnosis of Carcinoma of the Stomach. Herman J. Moersch and B. R. Kirklin. *Gastroenterology* 7: 285-291, September 1946.

In the opinion of the authors roentgen examination is preferable to gastroscopy as a routine procedure in the diagnosis of cancer of the stomach because of its ease of performance, rapidity, greater safety and the fewer contraindications to its use. Gastroscopy is of extreme value as an adjunct to roentgen and clinical examination in the study and diagnosis of carcinoma especially in those cases in which the roentgen findings are indistinct or at variance with clinical observations. The results of the two procedures in a selected series of 100 cases are presented and three illustrative cases are recorded. The close collaboration of the gastroenterologist, roentgenologist and gastroscopist is of great importance in bringing about the earlier diagnosis of gastric cancer.

Gastric Polyposis. J. H. Rapoport. New Orleans M. & S. J. 99: 71-78, August 1946.

Gastric polyposis, while rare, should be considered in the differential diagnosis of ulcer, carcinoma and benign tumors of the stomach. The author presents a brief historical review and discusses at some length the etiology, evaluating carefully the plausibility of the theories for both congenital and inflammatory origin. There is shown a definite relationship between gastritis, adenoma and carcinoma of the stomach. The high incidence of achlorhydria in patients with gastric polyposis suggests a relationship also to pernicious anemia and statistics bear this out, showing a greatly increased incidence of polyposis in the presence of that disease.

Pathologically polyposis is of two general types. In *polypadenoma polypaeux* there are many discrete polyps scattered over the gastric mucosa. They are usually pedunculated and many bear cysts. The other common type is the *polypadenoma en nappe*. In this type the hypertrophy forms a well demarcated plaque, not cystic or pedunculated. It is composed of closely

placed folds of hypertrophic mucous membrane resembling the convolutions of the brain

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that the third fluid level was just distal to the duodenojejunal flexure. At operation the site of obstruction was found to be the beginning of the jejunum which turned sharply to the right under the mesenteric vessels. It then spiralled around the mesenteric vessels in a clockwise direction for three complete turns. After the volvulus was corrected the rare condition of the jejunum piercing the mesentery of a lower loop was found. The cecum was in the left hypochondrium and was adherent to the splenic flexure by peritoneal bands. The mesentery of the ascending colon was adherent to the transverse mesocolon. An anastomosis was made between the third part of the duodenum and the jejunum distal to the point where it pierced the mesentery. The cecum and ascending colon were separated from the transverse mesocolon and a colectomy was performed. The child made an uneventful recovery and postoperative radiological examination showed a normal stomach and duodenum.

The second patient was a woman aged 49 years who had signs and symptoms of intestinal obstruction. Examination revealed abdominal distention and shifting dullness in the flanks. At operation the cecum was found to be distended and to have undergone a twist through 180 degrees around the ascending colon. After the volvulus was corrected the ascending colon was found to enter a retroperitoneal tunnel and then extend upwards and to the left behind the root of the mesentery and the mesenteric vessels to emerge at the normal splenic flexure. The patient died after thirty-six hours from pulmonary embolism.

MAX CLEMAN, M.D.

Lymphoblastoma of the Terminal Ileum. Anthony C. Gilluccio. *New York State J. Med.* 46: 2049-2052, Sept. 15, 1946.

A case is reported of lymphoblastoma of the terminal ileum which produced a filling defect in the cecum as a result of intussusception. The patient had symptoms of abdominal pain, cramp-like and severe in the right side of the abdomen on four occasions in eight months prior to entry. Physical and laboratory findings were not significant. The x-ray observations are carefully described and illustrated. The significant feature was the persistent intraluminal filling defect in the cecum. The appendix was directed downward and medially. The terminal ileum did not fill. A subsequent examination showed a higher implantation of the cecum with a curvilinear retention of barium at its base. The filling defect previously observed was less clearly defined.

The patient was operated upon and a large elevated lesion and two smaller lesions were noted in the terminal ileum which had slipped through the ileocecal valve into the cecum. The intussusception was reduced and the terminal ileum and cecum were resected. The diagnosis was lymphosarcoma of the terminal ileum of the reticulum-cell type. The patient died after suffering numerous postoperative complications and autopsy confirmed the diagnosis.

The author points out that some 400 cases of this type have been reported but that the histogenesis is obscure and differentiation from a benign lesion is frequently impossible. Lymphosarcoma is essentially a non-surgical disease except when it originates in the gastrointestinal tract and here the site influences the prognosis considerably. In lymphosarcoma of the stomach gastric resection is believed to offer a better prognosis than in carcinoma. Lymphosarcoma in the

jejunum and ileum forbodes a very poor prognosis as does a primary lesion of a similar nature in the rectum. If the lesion is located in the cecum the prognosis is much better and about a 50 per cent survival can be expected.

In reviewing his case report the author points out that one thing which might have suggested the preoperative diagnosis of lymphoblastoma rather than carcinoma was the fact that the patient suffered none of the manifestations which are normally expected with carcinoma of the cecum. The age of the patient (the third decade) and the absence of anemia were also against a diagnosis of carcinoma.

SYDNEY F. THOMAS, M.D.

Familial Diverticulosis of the Colon. Report of Seven Cases in One Family of Nine Persons. Harold I. Schlotthauer. *Ann. Surg.* 124: 497-502, September 1946.

Both gross and microscopical examination of the verticals of the colon show them to be herniations of the mucosa and submucosa through defects in the muscle layer of the bowel. These are usually at the points of entrance of blood vessels. The author reviews the current literature and theories explaining why these herniations occur. He then presents evidence why he believes heredity should be considered as a major etiological factor.

A study is reported of a family consisting of seven brothers and two sisters ranging in age from forty-nine to seventy years. Although diverticula were demonstrated roentgenographically in all seven males, only two of them had ever had symptoms referable to the colon. The seven men showed a wide variation in size and weight as well as in social status and habits of living so that there was no apparent common feature of etiology other than ancestry. No evidence of diverticulosis could be demonstrated in either of the two sisters.

STANLEY H. MACHT, M.D.

Roentgenological Evidence of Appendiceal Abscesses. Arthur Drillos. *Am. J. Digest. Dis.* 13: 279-284, September 1946.

The x-ray examination is often the decisive factor in establishing a diagnosis of appendiceal abscess. This is particularly true where the abscess follows weeks or months after subsidence of acute abdominal symptoms or in cases of a chronic type in which as a result of a suppurative infection the appendix has been perforated and become walled off producing a localized abscess with tumor formation.

The author discusses several cases of appendiceal abscesses. The symptoms were varied but in each instance a deformed cecum was demonstrable on barium enema films taken both before and after evacuation. The points of diagnosis are as follows: (1) filling defects either extrinsic or intrinsic or both; (2) fixation of cecum and last loop of ileum; (3) elevation and displacement of ileum; (4) hyperirritability and hypermotility with cecal spasm; (5) sensitiveness and tenderness of the area; (6) failure to visualize the appendix.

Conditions to be differentiated are carcinoma of the cecum, ileocecal tuberculosis, regional ileocolitis, actinomycosis and invagination with intussusception. Extra-intestinal conditions such as pelvic abscess and paranephritic abscess are also worth considering.

JOSEPH T. DANZER, M.D.

THE MUSCULOSKELETAL SYSTEM

Juvenile Rheumatoid Arthritis A Study of Fifty-Six Cases with a Note on Skeletal Changes James A. Coss, Jr and Ralph H. Boots J Pediat 29 143-156, August 1946

Fifty six cases of rheumatoid arthritis in children have been observed at Columbia Presbyterian Medical Center (New York) since 1928. This group includes those cases in which the onset was at twelve years of age or earlier and represents 4.9 per cent of all cases of rheumatoid arthritis seen. The term Still's disease is not used as there seems to be no justification for this special grouping. In 18 instances (32 per cent) a family history of possibly related conditions was obtained. Thirty two patients (57 per cent) had a history of respiratory tract infection including pneumonia, bronchitis, recurrent sore throat, sinusitis or otitis preceding or associated with the onset of the arthritis. Thirty nine patients (69 per cent) had a history of frequent ear, nose and throat infections at some time in the course of the illness. Seven patients (12.5 per cent) had a preceding or concurrent history of gastro intestinal disturbance. Only one patient had previously had rheumatic fever.

Thirteen patients had hepatomegaly, 17 splenomegaly and 35 generalized lymph node enlargement of varying degree. The reported lack of pain in Still's disease was not characteristic of this series. Practically every patient at some time complained of pain. In 31 cases no cardiac abnormality was discovered on physical examination or electrocardiography. 13 patients had tachycardia, 13 a systolic murmur of varying intensity (never harsh) and in 7 instances the electrocardiographic variation was great enough to be diagnosed as evidence of myocardial damage or "carditis." In 6 cases this reverted to normal on subsequent study. About 80 per cent of the patients showed a moderate anemia. In 37 per cent on the basis of the highest figure recorded the leukocyte count was above 15,000 and in 17 per cent it was above 25,000. The many similarities between rheumatic fever and rheumatoid arthritis lead to the interesting conjecture that recurrent hemolytic streptococcal infection and its consequences may play a part in rheumatoid arthritis as has been suggested in the former condition.

Four roentgen criteria which seem to be most characteristic of juvenile rheumatoid arthritis (see Taylor *et al* Arch Int Med 57 979 1936) were selected: *vis* decalcification, bone destruction, joint space narrowing and soft tissue changes. X ray studies were available in 47 patients and in each instance at least one of the above criteria was present. In 20 cases two items were present, in 9 three and in 7 all four changes were demonstrable. As would be expected more marked changes were seen in the older patients who had had the disease for a longer time. Joint changes as evidenced roentgenographically are often rather late to appear just as in adult rheumatoid arthritis. Although some writers consider the roentgen picture of juvenile rheumatoid arthritis identical with that of rheumatoid arthritis in adults, additional features peculiar to arthritis in the young age group were noted in the present series. Many observers have remarked about the generalized failure of maturity and the bird-like facies in juvenile arthritis. Some films in this series showed a fusion of cervical vertebrae following arthritis. This change in children has usually been

spoken of as congenital failure of segmentation, but the authors consider it a bony fusion resulting from arthritis in the involved area. Other patients showed brachydactylia. Twenty-two of the 56 patients were found to have disturbed skeletal patterns of varying degree.

Numerous forms of therapy were tried, with variable response. Twenty two patients received gold (average course 600 mg gold compound) as well as other measures of treatment. Because of the small number of cases, however, and the extreme variation in total dosage it has been impossible to evaluate comparatively the response to this form of treatment.

Typical cases are reported including the two fatalities. One of the fatal cases exhibited terminal amyloidosis.

Case of Albright's Syndrome (Osteitis Fibrosa Disseminata) R. C. Murray, H. J. R. Kirkpatrick, and Elemér Forrai Brit J Surg 34 48-57 July 1946

The authors give a review of the literature on Albright's syndrome and report a case in which the diagnosis was based on the combination of progressive fibrous dysplasia of bone beginning early in life, the radiologic and histologic appearances of the osseous lesions, absence of changes in the blood chemistry characteristic of parathyroid adenoma, and pigmentation of the skin.

The patient was a man of 22 whose family history was negative for deformity. When he was four years old it was discovered that he was knock-kneed, but medical advice was not sought until the age of nine. At that time the condition had become much worse. A wedge osteotomy was performed on the left tibia and fibula and union was apparently normal. A fracture of the left femur as a result of slight trauma the following year also healed normally, but the deformities of the lower extremities grew steadily worse until in another year walking was impossible. At the time of examination by the authors there were fantastic deformities of both lower extremities with gross bowing of the upper end of each femur, hyperextension deformities of both knees and calcaneus deformities of both feet. The shaft of each tibia in addition to showing a hairpin bend was thickened. There was a large area of brown pigmentation covering the greater part of the left side of the body from the level of the iliac crest below to the nipple line above.

X ray examination of the skeleton showed that both sides of the body were equally affected, the lower half being far more extensively involved than the upper half. The entire tibial shaft was involved showing deformity, expansion, thinning of the cortex, decalcification and a honeycomb of apparently cystic spaces of varying sizes. The femurs showed similar changes but with areas of normal bone between. The other long bones contained one or more cystic areas and the shafts were decalcified but otherwise normal. There were no calculi in the kidneys. Plasma inorganic phosphorus was low although in the cases recorded in the literature values have been within normal limits. Benace Jones protease was found on several occasions. Calcium metabolism experiments were essentially normal.

This patient was treated for correction of deformities by multiple osteotomies. It was found that union took place within normal time limits even when the osteotomy was through a cystic area. These areas are not

replaced by bone and it is therefore advisable to excise contents of cysts and fill with bone. The pathological examination of the excised bone revealed that the consistency and structure of normal bone were lacking. The tissue was soft and cut easily. In some parts it consisted of soft fibrous tissue covered by a thin shell of cortical bone. In other parts there were areas of compact porous bone and areas of coarse and fine honeycomb structure. Histologic examination showed numerous irregularly formed and imperfectly calcified trabeculae of osseous tissue in a matrix of cellular connective tissue. The cortical zone was narrow. Bone formation and resorption were in active progress.

The etiology of the disease is theoretical. The authors of the present paper believe that the lesions are secondary to some extraskelletal disorder of endemio-phosphorus metabolism, a part of a congenital anomaly with an incidental localizing mechanism partly congenital and partly acquired. In parathyroid adenoma in addition to the generalized decalcification of the skeleton there are multiple foci of osteitis fibrosa which are presumably related to incidental factors of localization. Such incidental factors may be of a similar kind to those which determine the localization of the bone lesions in Albright's syndrome.

MAX CRIMAN, M.D.

Periarthritis of the Shoulder J. D. McInnes. *Canad. M. A. J.* 55: 131-133 August 1946.

Chronic adhesive subacromial bursitis commonly called frozen shoulder, causes pronounced limitation of shoulder function. The lack of understanding of the basic etiology has led to much ineffective treatment.

Persistent shoulder pain radiating up the neck or down the arm or loss of motion may bring the patient to the physician. In addition to pain there may be tenderness around the joint capsule, muscle atrophy, and limitation of active and passive motion. The appearance of the arm, wrist and hand may be similar to that in hemiplegia or rheumatoid arthritis. X-ray examination usually reveals generalized decalcification of the bones of the shoulder girdle, and occasionally calcium deposits may be seen in the subacromial bursa.

Two typical cases are reported in which the essential therapy consisted in forceful manipulation of the involved shoulder under anesthesia on two or more occasions, followed by a definite routine of passive and active motion physiotherapy and increasingly intensive exercise. Gradually the range of movement increased and the pain on motion decreased. After a year, one patient had a normally functioning and painless shoulder, and the other patient was progressing favorably.

W. P. MARTIN, M.D.

GYNECOLOGY AND OBSTETRICS

Maternal Obstetric Paralysis John Totterdale Cole. *Am. J. Obst. & Gynec.* 52: 372-386 September 1946.

Maternal obstetric paralysis or traumatic puerperal neuritis is a condition observed during the puerperium and occasionally during labor. It is characterized by pain and paresthesias and a variable paralysis of one or both of the lower extremities. The condition is rare but early diagnosis and treatment are important.

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obscured by sedatives and analgesics. As uterine contractions become more intense the pain increases. It may be associated only with uterine contraction.

Various paresthesias occur and the patient may complain of numbness, 'pins and needles' or thermal changes. Spasmodic contractions or paralysis of muscles may be observed. The degree of nerve involvement varies, but 'foot drop' is a rather constant finding, and other muscles of the leg and thigh are involved. The ankle and knee jerks may exhibit abnormalities while sensory findings will range from almost normal to complete loss. In severe cases atrophy and wasting of muscle groups will eventually follow. To be differentiated are localized bone or muscle changes, stirrup injuries, embolism, tumors, and infectious poisoning, hysteria, and herniated disk.

After reviewing the various theories as to the etiology, the author concludes with Barnes (J. Obst. & Gynec. Brit. Emp. 50: 13, 1943) that the paralysis is chiefly due to trauma of the lumbosacral cord by the fetal head or by instruments, a view first propounded by Hünnermann. In many cases cephalopelvic disproportion exists. In a pelvis in which the x-ray findings show that the posterior ilium is short, the ala of the sacrum has only a shallow anterior concavity, and the promontory does not encroach on the capacity of the posterior segment, it seems reasonable that that portion of the vertex in relation to the ala can exert real pressure on the lumbosacral cord when the fetal head seeks an obliquity. This is why barring instrumental injury, the lesion is almost exclusively unilateral. Pain and other symptoms appear rather late in labor because the head exerts its greatest pressure on the nerve cord at the time of engagement and at the height of a uterine contraction.

In those cases attributed to instrumental manipulation, the degree of damage depends not only on the short period of compression by the posterior blade but also on the amount and force of the traction used.

The author reports in detail seven cases including polymeric studies before delivery and an x-ray review postpartum after obstetric paralysis had been diagnosed. The x-ray findings though characteristic are not diagnostic for pelvis with these features are seen in which no nerve trauma occurs.

Early signs of lumbosacral cord compression should be watched for in trial labors and their appearance necessitates extreme care in further management. Treatment consists of support of the injured extremity, active and passive motion, galvanic stimulation, vitamin therapy, and the use of a walking brace. Prognosis as to the degree and speed of recovery should be guarded.

WILLIAM P. MARTIN, M.D.

Variations in the Female Pelvis C. Nicholson and H. Sandemann Allen. *Lancet* 2: 192 Aug. 10, 1946.

The authors criticize the Caldwell-Moloy classification because of its lack of precision. They say, "Classification may be a fine weapon in the armament of science, but classification without precise definition is simply the negation of science and can only lead to the multiplication of types until every example has a type of its own." They point out that Caldwell and Moloy already have thirty types. They seek to disprove the facts that (1) the android pelvis is a male pelvis associated with other male stigmata in the female, (2) that the android pelvis and to some extent the anthropoid

pelvis are associated with narrow outlets, (3) that the android pelvis is associated with difficult labor. They produce evidence that they feel disproves these propositions, which they say Caldwell and Moloy have propounded. They attempt to produce statistical proof that the android pelvis is associated neither with contraction of the pubic angle, nor with difficulty in labor, and point out that any deformities of the pelvis which lead to difficult labor are due to deficient nutrition in childhood.

Whereas Caldwell and Moloy have wished to emphasize the shape rather than the size of the pelvis the present writers apparently wish to reverse this and go back to the old idea that size alone counts. [An editorial discussion of this subject, with a critical evaluation of the opposing views, appeared in *Radiology* for May (48 527 1946).] PAUL C SWENSON M D

Pelvimetry E P Allen New Zealand M J 45 370-375 August 1946

The author seeks to answer the question "Upon what criteria can we predict a normal labor?" His technic calls for five films (1) an anteroposterior film with the patient supine, with a firm pad under the concavity of the lumbar spine, (2) a localized double exposure film of the pelvis with full stereoscopic shift of the tube between exposures, (3) a lateral soft-tissue film of the uterus, (4) a lateral view of the bony pelvis with markers anteriorly and posteriorly in the mid line, (5) a film of the subpubic angle after the method of Chassard and Lapiné. The stereoscopic reconstruction method of Caldwell and Moloy is not looked upon with favor. Such a method, the author believes can be accurate only after years of experience.

The pelvis is measured at three levels: the inlet, the midplane, and the outlet. At the inlet the two main diameters to be measured are the transverse and the obstetrical conjugate. Of the latter the author says "There is no doubt that in some cases the classical conjugate does not represent the available anteroposterior diameter." As an example he cites the extreme case of a sacrum in which the first segment is largely lumbarized and the pubosacral angle is much less than 90 degrees. In such a pelvis it is clear that the 'least' conjugate (from the upper border of the symphysis pubis to the nearest point on the sacrum) rather than the classical conjugate represents the available sagittal plane diameter. When the pubosacral angle is greater than 90 degrees however the classical conjugate is also the least conjugate. In view of these considerations the author measures the classical conjugate unless the angle is under 90 degrees in which case the least conjugate is measured. Considering the two major diameters as the two axes of an ellipse the brim area can be derived from the formula $\pi \frac{ab}{4}$ where a and

b are the two diameters. On the basis of his experience the author considers a conjugate of 100 mm in New Zealand at least an absolute indication for cesarean section in the case of the average fetal head.

At the midplane or the least pelvic plane the usual diameters measured are the anteroposterior and the bispinous. As with the inlet the two diameters can be regarded as the major and minor axes of an ellipse and the midplane area can be calculated accordingly. Nicholson is quoted as fixing the critical area of the midplane at 90 sq cm and the author's experience is in

good agreement with this figure. In 35 per cent of his cases the bispinous diameter was below 100 mm. He feels, however, that this diameter lies too far posterior to seriously affect delivery since one must assume the head to be fully flexed and molded by the time it reaches this area. He suggests, as more useful, a transverse measurement anterior to the bispinous diameter, as the distance between the flat opposing surfaces of the bodies of the ischia in front of the spines. He sets down as a criterion for midplane contraction a critical area of 103 sq cm calculated from the anteroposterior and true transverse diameters. The bispinous diameter is of significance only if it is less than 100 mm and lies well forward as shown by a relatively long posterior sagittal diameter.

Consideration of the outlet has generally been confined to measurement of the subpubic angle and a so-called bituberous diameter. Measurement of the subpubic angle is, however, inaccurate, and the bituberous diameter has no clearly defined end point. Furthermore neither measurement has any particular significance unless it is related to the position of the tip of the sacrum. The author offers what he believes is a new approach to this problem. He superimposes upon the film of the subpubic angle a transparency consisting of a half circle 10.4 cm in diameter which is taken to represent the anterior half of the fetal head with a slight allowance for enlargement on the film. This transparency is so placed that the circle touches each side of the subpubic arch and the scale with which it is provided passes through the symphysis. The symphysis biparietal distance as read off on the scale represents the least distance behind the lower edge of the symphysis at which the greatest transverse diameter of the head can negotiate the subpubic arch and is the measure of the space under the subpubic arch required for the anterior half of the head. To determine whether the sacrum will interfere with delivery of the posterior half the symphysis-biparietal distance is increased proportionately to allow it to be fitted to the lateral film. This magnified distance is taken off on a compass and with the center on the lower edge of the symphysis an arc is described across the tuberosities. This represents the locus of the greatest transverse diameter of the head. Where the arc intersects the ischiopubic ramus or the posterior surface of the tuberosities a mark is made. The distance of this mark from the sacral tip is measured and corrected for divergent distortion and is the available posterior sagittal outlet. To permit delivery of a normal head this diameter must be more than 50 mm.

In summary the following critical limits are listed

Inlet area	110 sq cm
Obstetrical conjugate	110 mm
Midplane area	103 sq cm
Posterior sagittal outlet	50 mm

SYDNEY F THOMAS M D

Six Cases of Venous Intravasation Following Intra-uterine Lipiodol Injection Alice Bloomfield J Obst & Gynec Brit Emp 53 345-346 August 1946

Conditions predisposing to venous intravasation following intrauterine injection of lipiodol for salpingography are said to be (1) injection of lipiodol within a period of less than eight days after the termination of menstruation (2) injection immediately after dilatation of the cervix (3) injection too soon after curet-

replaced by bone and it is therefore advisable to excise contents of cysts and fill with bone. The pathological examination of the excised bone revealed that the consistency and structure of normal bone were lacking. The tissue was soft and cut easily. In some parts it consisted of soft fibrous tissue covered by a thin shell of cortical bone. In other parts there were areas of compact porous bone and areas of coarse and fine honeycomb structure. Histologic examination showed numerous irregularly formed and imperfectly crisped trabeculae of osteoid tissue in a matrix of cellular connective tissue. The cortical zone was narrow. Bone formation and resorption were in active progress.

The etiology of this disease is theoretical. The authors of the present paper believe that the lesions are secondary to some extraskeletal disorder of calcium phosphorus metabolism, a part of a congenital anomaly, with an incidental localizing mechanism partly congenital and partly acquired. In parathyroid adenoma, in addition to the generalized decalcification of the skeleton, there are multiple foci of osteitis fibrosa, which are presumably related to incidental factors of localization. Such incidental factors may be of a similar kind to those which determine the localization of the bone lesions in Albright's syndrome.

MAX CLIMAN, M.D.

Periarthritis of the Shoulder J. D. McInnes
Canad. M. A. J. 55: 131-133, August 1946

Chronic adhesive subacromial bursitis, commonly called "frozen shoulder," causes pronounced limitation of shoulder function. The lack of understanding of the basic etiology has led to much ineffectual treatment.

Persistent shoulder pain radiating up the neck or down the arm, or loss of motion, may bring the patient to the physician. In addition to pain there may be tenderness around the joint capsule, muscle atrophy, and limitation of active and passive motion. The appearance of the arm, wrist and hand may be similar to that in hemiplegia or rheumatoid arthritis. X-ray examination usually reveals generalized decalcification of the bones of the shoulder girdle, and occasionally calcium deposits may be seen in the subacromial bursa.

Two typical cases are reported, in which the essential therapy consisted in forceful manipulation of the involved shoulder under anesthesia on two or more occasions, followed by a definite routine of passive and active motion, physiotherapy and increasingly intensive exercise. Gradually the range of movement increased and the pain on motion decreased. After a year, one patient had a normally functioning and painless shoulder and the other patient was progressing favorably.

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epithelial lining of the ducts and acini. There are swelling and narrowing of the ducts, epithelium is shed, and the outlet for the contents of the acini is blocked. As a consequence there is stagnation of the intra-acinar exudate and dilatation of the acini. Then follows reactive new formation of connective tissue around the affected acini. At this stage the gland usually responds readily to simple treatment, as massage, heat, etc., unless it is constantly reinfecting from some focus. If the inflammation is more severe and lasts long enough the dilatation of the acini progresses, the intra acinar septa are broken down, resulting in the formation of larger cavities. In the periphery of the affected area new connective tissue is formed, and finally irregular, ramified large cavities surrounded by dense fibrous tissue may develop. These cavities are connected with the posterior urethra through dilated prostatic ducts which, however, are not wide enough to allow a good drainage of the cavities. Furthermore, any urethral obstruction distal to the prostate will tend to dilate the cavities by back pressure. This is in agreement with the fact that prostatic diverticula are found most frequently in cases of stricture of the urethra of long standing. By the contact of urine with debris in the cavities, salts may be precipitated and prostatic stones develop. These may block the ducts and so, again, contribute to the growth of the cavities.

These cavities or prostatic diverticula, take a considerable time to develop, often five or ten years or longer. Usually they produce only slight symptoms or none at all. They constitute, however, a locus minoris resistentiae ready to flare up if more virulent organisms enter. Then the infection may spread rapidly and affect the whole urinary system. In rare cases even septicemia may develop.

The diagnosis of prostatic diverticula can be made only by x ray or urethroscopic examination. The x ray film does not always show the cavities. The contrast medium sometimes fails to penetrate through the prostatic ducts into the diverticula or the shadow of the urethra may overlap a small diverticulum. Films in at least two projections are therefore desirable. If no diverticula are found by the usual technic of urethrography, they may still be visualized by the following procedure. After introduction of the contrast medium into the bladder the patient is asked to void and at the same time his urethra is compressed and the x ray film is taken. The urethroscope shows the dilated ducts leading to the diverticula very well but does not give information about their size and direction. Therefore, both methods should be applied.

Treatment by opening and drainage of the pus cavities is outlined by the author. His procedure of choice is transurethral endoscopic incision of the cavities with high frequency current. He indicates that some cases are suitable for the resectoscope especially those complicated by sclerosis of the bladder neck. Open operation transvesical or perineal is not advised as a routine procedure as in most cases satisfactory results can be obtained by simpler methods.

MARLYN W. MILLER, M D

Roentgen Examination of the Male Urethra
Howard Gaudin New Zealand M J 45 376-383
August 1946

The author points out that the roentgen examination of the male urethra is not widely practised despite the

fact that it can sometimes demonstrate disease which cannot be diagnosed in any other manner. His method is a modification of that described by Kohnstam and Cave (*Radiological Examination of the Male Urethra*, New York, Wm Wood & Co, 1925). He uses as a contrast medium a 40 per cent suspension of barium sulfate in water with gum tragacanth in the proportion of 0.5 to 1.0 per cent, and obtains two views one before and one after injection, both in the right oblique position. The method of injection is that used by Kohnstam and Cave. A conical glass flask constitutes an air pressure reservoir and air pressure is created by means of a sphygmomanometer bulb. This reservoir is connected to a mercury manometer and to the barrel of a glass dressing syringe large enough to contain medium for several examinations. The pressure at which the sphincter vesicae relaxes may be noted and one may watch the flow of the medium and time the exposure so that it is made while the barium mixture is flowing in the urethra.

Three main entities are discussed: the normal picture, the strictured urethra and the enlarged prostate. The normal measurement of the prostatic urethra is the distance between the verumontanum and the neck of the bladder, which is approximately 2.0 cm, but enlargement of the prostate increases this distance.

The illustrations accompanying the paper are excellent and, as is so frequently the case, present the subject more effectively than any written description.

SYDNEY F. THOMAS, M D

SINUS TRACTS

Injection of Iodized Oil as an Aid to Closure of Draining Sinuses. George Crile Jr U S Nav M Bull 46 1174-1177, August 1946

An unrecognized sinus is one of the most common causes of failure of a wound to heal. It is suggested by gray edematous granulations bathed in pus. If a sinus persists for several weeks, one must always suspect that it contains foreign material, enters a hollow viscus (fecal fistula), or is kept open by a poorly drained abscess cavity or a piece of infected bone. When the drainage is profuse a non-metallic foreign body or a piece of necrotic bone is probably present.

After the presence of a sinus is established a roentgenogram should be taken to rule out osteomyelitis, sequestra or metallic foreign bodies. If these are not present, iodized oil should be injected under fluoroscopic control and the tract filled. Roentgenograms are then taken either stereoscopically or from both anterior posterior and lateral angles to determine the extent of the tract. No attempt is made to retain the oil in the wound. If the x rays show no obvious cause for the sinus there is better than even chance that the sinus will close within one or two days following the injection of the oil and remain closed. If the drainage persists it is often worth while to give penicillin both locally and systemically and after two days to reinject the sinus with iodized oil. The penicillin is given for two days more and in many instances closure of the sinus will ensue.

The iodized oil often remains in the tissues for several months and can be demonstrated by x ray despite the fact that the sinus is closed.

Within a year the author had observed closure of approximately 20 large sinuses following the injection of iodized oil. Eight brief case reports are presented.

tage, (4) injection just prior to the onset of menstruation and (5) injection with excessive force

Six cases in which pelvic venous intravasation occurred are analyzed with these contraindications in mind. In one patient salpingography was carried out just after the end of the menstrual period. Films showed one tube to be freely patent and the other possibly blocked at the cornua with intravasation of dye into the pelvic veins. The patient felt no ill effects at the time, although a roentgenogram of the chest showed fine flecks of scattered lipiodol. After returning home, however, she experienced prolonged irregular vaginal loss, followed by a heavy period "suggesting a mild pelvic inflammatory reaction." Salpingography was carried out in the second patient four to five days before the onset of menstruation and excessive pressure may have been used. The degree of intravasation of the pelvic veins was marked. A chest film was not taken for two or three weeks, and at that time the lung fields were clear. In 3 cases the intravasation was attributed to a new and rather rough surfaced rubber covering to the oil bearing cannula, this having presumably traumatized the cervix and permitted the ingress of lipiodol to the pelvic veins. All 3 of these patients had hemoptysis and a roentgenogram of the chest in each instance showed a very fine faint stippling giving a granular appearance through both lungs. The possibility that this was due to lipiodol in minute quantities in the terminal capillaries is suggested. No cause for the intravasation was evident in the sixth case.

GENITO-URINARY SYSTEM

Intravenous Urography in Acute Renal Colic
Thomas J. Florence, William S. Howland, and H. Stephen Weeks. *J. Urol.* 56: 284-291, September 1946.

The point is made that despite voluminous literature concerning renal colic, little attention is given to the early diagnosis of its underlying causes. The authors feel that in addition to the usual procedures such as urinalysis and survey roentgenograms, intravenous urography should be employed more frequently as an early diagnostic measure. Hematuria is not always conclusive evidence of colic and the survey roentgenogram frequently has to be supplemented by further studies for diagnosis or verification. Cystoscopy and retrograde pyelography are not considered practical for immediate routine procedure.

Intravenous urography was performed in 23 patients during episodes of acute renal colic. In a number of these cystoscopy and retrograde pyelography were also done for better evaluation of the intravenous urography. In 12 of the patients calculi were found to be the cause of the colic. In the remainder ureteral stricture, kinking of the ureters and congenital anomalies of the urinary tract were considered as etiologic factors. In only one case were there no abnormal urographic findings.

Opacification of the kidney (nephrogram) during intravenous urography is stressed as a sign of ureteral blockage. This was observed in 10 cases, 5 of which were due to calculous and the remainder to non-calculous obstruction. The authors explain the phenomenon of opacification as follows: In complete ureteral obstruction the intrarenal pressure gradually rises to a level at which glomerular filtration is suppressed. The tubular epithelium, however, in spite of

ureteral obstruction retains its function and may excrete diodrast which accumulates in the tubular apparatus leading to a diffuse opacification of the renal shadow on intravenous urography. As soon as the obstruction is relieved the contrast medium passes readily from the tubules into the kidney pelvis and the renal shadow returns to normal. The phenomenon may be artificially produced. Further work in connection with nephrography is to be published.

DAVID S. MALEN, M.D.

Ditopax, A New Excretory Urographic Medium. A Clinical Report on 1280 Injections. W. M. Kearns, Hans Hefke and S. A. Morton. *J. Urol.* 56: 392-398, September 1946.

Ditopax (Bis diethanolamine λ methyl-3,5-diiodo-chelidamate) was used for 1280 injections in 1,232 patients. Blood chemistry and blood pressure determinations, electrocardiograms and urinary iodine excretion estimations were obtained in a group of 10 patients. In addition, a comparison was made of radiographic densities with Ditopax, Neo-iopax and Diodrast in groups of 10 and 7 patients. Composite observations for Ditopax reactions on 915 patients are tabulated.

The conclusions reached are as follows: (1) Ditopax is safe. (2) Of 915 patients 75 per cent showed no reaction, 25 per cent showed inconsequential reactions. (3) The diagnostic value is rated in the following order: Neo-iopax, Ditopax, Diodrast. (4) On the basis of this series, Ditopax may be said to cause less arm pain than Neo-iopax and less systemic reaction than Diodrast.

PAUL R. NOBLE, M.D.

Diverticula of the Prostate. Ernest Hock. *J. Urol.* 56: 353-367, September 1946.

Nine cases are presented illustrating the diagnosis by urethrography and urethroscopy of chronic diverticular prostatitis and its treatment by transurethral electroincision.

During the past decade the importance and frequency of chronic prostatitis have become more and more recognized. Little attention has been given, however, to a certain form of prostatitis characterized by the formation of diverticula. These prostatic diverticula are not very rare and have been repeatedly described and discussed by such writers as Luys, Chevassu, Thompson, Michel and others. The best account is given by Heitz-Boyer of Paris who studied in detail the pathology, development, clinical importance and treatment of prostatic diverticula. [References to his numerous papers are included.]

Prostatic diverticula may develop from any "simple" prostatitis. The portals of infection are (1) from the posterior urethra through the prostatic ducts, (2) from the epididymis through the ejaculatory ducts, (3) through the blood stream, metastatic, (4) through the lymphatics from adjoining organs. Lymphogenous infection plays a comparatively unimportant role. Infections from the testicle and epididymis through the vas deferens occur but are not frequent. In most cases the bacteria enter the gland either from the urethra or through the blood stream. Often there is an infectious focus, removal of which is followed by healing of the prostatitis.

Irrespective of the mode of bacterial invasion of the prostate, the first pathological changes take place in the

epithelial lining of the ducts and acini. There are swelling and narrowing of the ducts, epithelium is shed, and the outlet for the contents of the acini is blocked. As a consequence there is stagnation of the intra acinar exudate and dilatation of the acini. Then follows reactive new formation of connective tissue around the affected acini. At this stage the gland usually responds readily to simple treatment, as massage, heat etc., unless it is constantly reinfected from some focus. If the inflammation is more severe and lasts long enough the dilatation of the acini progresses, the intra acinar septa are broken down, resulting in the formation of larger cavities. In the periphery of the affected area new connective tissue is formed, and finally irregular, ramified, large cavities surrounded by dense fibrous tissue may develop. These cavities are connected with the posterior urethra through dilated prostatic ducts which, however, are not wide enough to allow a good drainage of the cavities. Furthermore any urethral obstruction distal to the prostate will tend to dilate the cavities by back pressure. This is in agreement with the fact that prostatic diverticula are found most frequently in cases of stricture of the urethra of long standing. By the contact of urine with debris in the cavities, salts may be precipitated and prostatic stones develop. These may block the ducts and so again contribute to the growth of the cavities.

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Within a year the author had observed closure of approximately 20 large sinuses following the injection of iodized oil. Eight brief case reports are presented.

FOREIGN BODIES

A Simple and Accurate Method for the Localisation of Intra-Ocular Foreign Bodies G I Scott and P A Flood Brit J Radiol 19 318-322 August 1946

If an opaque intra ocular foreign body is suspected, a preliminary film is made in the postero anterior position with the head slightly extended so that the petrous pyramid shadow will fall below the orbit. If a foreign body is visualized a second postero-anterior projection is made. This is a double exposure the first made with the eyes fixed straight ahead and the second with the eyes looking about 20 degrees downward. If the shadow of the foreign body shifts it is

either in the globe or in contact with the sclera. Accurate localization is then in order. A ring of thin silver wire perforated at 12 and 6 o'clock is sutured to the limbus. It is not necessary to locate these perforations at exactly 12 and 6 o'clock but a mark should be made on the sclera opposite each with a small needle dipped in Chinese ink. Two exposures then are made, a postero anterior and a direct lateral with the eyes fixed straight ahead. From these two films the localization of the foreign body may be charted on a diagram with greater accuracy than the surgeon needs. The marks on the sclera are sufficient guides for him.

The technique of surgical removal of the foreign body is also described. SYDNEY J HAWLEY M D

RADIOTHERAPY

NEOPLASMS

Radiation Treatment of Cerebral Tumors R McWhirter J Pennybacker, Dorothy S Russell J Jackson Richmond *et al* Proc Roy Soc Med 39 673-680 August 1946

McWhirter reported a series of 115 histologically proved brain tumors treated with x rays between 1936 and 1944. In the majority of cases a decompression operation was carried out prior to the application of radiation. The treatments were usually given with radiation generated at 250 kv and filtered with a Thoraeus filter through two fields. A minimum tumor dose of 4 500 r in four weeks was planned but in some cases was not reached. In attempting to assess accurately the effect of radiotherapy clinical observation x ray studies further surgical exploration and postmortem studies were used.

Brain tumors were classified into four main groups. The first group numbering 23 consisted of the radio-insensitive tumors i.e. astrocytomas, ependymomas, oligodendrogliomas and radio-insensitive meningiomas and showed a 26 per cent five year survival. The survival rate did not differ materially from that for cases receiving no radiotherapy. There was no clinical proof that the tumor in these cases had diminished in size and tissue removed at a later date either operatively or at autopsy showed no significant effect of the irradiation. The five year survival rate is due to the naturally slow growth of these tumors. The rate of growth may have been slowed down to some extent by the irradiation.

The second group numbering 38 consisted of radiosensitive non metastasizing tumors and was made up of radiosensitive meningiomas, hemangioblastomas and neuro-epitheliomas. It showed a five-year survival rate of 61 per cent. The meningiomas formed the larger part of this group. The gross differentiation between radiosensitive and radio-insensitive meningiomas is not always easy nor can they be distinguished by histologic study in all cases. The author gives several descriptive points which may be of value in making a differentiation.

The third group—the radiosensitive metastasizing tumors—included the medulloblastomas, ependymoblastomas, malignant choroidal papillomas and pinealoblastomas. This group numbered 29 and the five year survival rate was 14 per cent. The tumors are highly radiosensitive but difficult to control because of their extreme tendency to metastasize to other

parts of the central nervous system. More recently localized treatment has been replaced by treatment over extensive fields including all of the cerebrospinal axis.

The fourth group was made up of those questionably radiosensitive tumors—the glioblastomas. None of the 25 patients survived five years.

The author says little about pituitary tumors except that the eosinophil tumors are suitable for x-ray therapy, which may bring about some improvement in the accompanying acromegaly. He also believes that basophilic pituitary tumors and craniopharyngeal carcinoma may be benefited to a considerable extent by irradiation.

The overall five year survival rate in the series reported was 27 per cent.

Continuing the discussion, Pennybacker emphasized the difficulties of assessing the value of irradiation in brain tumors. 'Have we really any evidence?' he asks, 'that radiation treatment has an effect on brain tumours?' To this query he replies 'I think anyone who has seen the response of a medulloblastoma to a course of x ray therapy would say yes. But even with these tumours it is a prolongation of life and not a cure which we achieve.' As to whether a cure is ever brought about by radiation he reports one case in which this seems to have been achieved—a malignant glioblastoma of the right frontal lobe. The patient died seven and a half years after the onset of symptoms, having received radium therapy and three courses of deep x ray therapy. No evidence of tumor was found at autopsy but there was an extensive subcortical necrosis maximal in the field of irradiation so it must be assumed that the radiation which killed the tumor was also responsible for the patient's death.

The histologic findings in this and a similar case are described by Russell who also reported some animal experiments to determine the nature of the changes induced by radiation.

The other discussants added brief remarks on the problems involved. B S KALAYJIAN M D

Radiation Therapy of the Cancer of the Esophagus. J Borak Am J Digest Dis 13 249-252 August 1946

That cancer of the esophagus is generally considered to be radioresistant is not easily explained as over 95 per cent of these tumors are of the squamous cell type and squamous-cell cancers in other parts of the

body are amenable to x-ray therapy Lacassagne, in experiments on animals, found that the epithelium of the esophagus behaved no differently than that of any part of the body Regaud and Coutard found that the squamous-cell covering of the skin and mucous membranes would degenerate when sufficient radiation was applied, but the underlying tissue would only exhibit signs of inflammation and the epithelium would eventually be regenerated from the neighboring areas

The fact that the esophagus has thin walls is a serious handicap in the use of radium because of the intense effect on adjacent tissues The difficulty of external irradiation lies in the distance of the esophagus from the surface It is roughly 8 to 12 cm from the chest wall in its middle and lower portions If 4,000 r is to be given to an esophagus, 10,000 to 12,000 r must be given to the skin This amount is difficult to apply without causing serious injury to the neighboring tissues A technique is described by the author in which 4,000 r is given to the tumor within four weeks For this purpose the patient is irradiated twice daily, six to eight hours apart At each session two fields each 5×12 cm are treated The wall nearer to the tumor has three fields parallel to one another, the opposite one has one to three fields depending upon the depth of the tumor At 200 kv, the single dose is 150 r to the skin

Two patients treated in the manner described are alive and apparently free from the disease, one for a period of seventeen months the other for twenty one months

JOSEPH T DANZER, M D

Unusual Metastatic Manifestations of Breast Carcinoma. I Metastasis to the Mandible with Report of Five Cases Frank E Adair and Julian B Herrmann Surg, Gynec & Obst 83 289-295 September 1946

Carcinomatous metastasis to the mandible is rare even from lesions which frequently produce osseous metastases, as carcinomas of the thyroid, prostate and breast Only 16 cases of carcinoma of the mandible secondary to mammary cancer including 5 presented in this paper have been recorded

The first indication of a metastatic tumor of the mandible may be pain frequently associated with a loose tooth Later a lump on the jaw may become apparent In 2 of the authors cases paresthesia of the side of the face and of the buccal and gingival mucosa developed some time before any other evidence of mandibular disease became apparent Although most mandibular metastases are associated with metastatic deposits in other bones there have been instances of a single metastasis localized to the mandible occurring a number of years after mastectomy for cancer Such a lesion may be mistaken for a primary growth and lead to an unwarranted radical procedure

In the cases reported roentgen irradiation usually gave some relief from pain and in one case regeneration of bone in the tumor area was noted

In an effort to explain the rarity of secondary carcinoma of the mandible the authors briefly review the classical theories of metastasis The theory of Pinner (Brit J Surg 10 235 1922) seems to be appropriate to this particular problem He believed that bone metastases are produced by blood borne emboli which lodge in the thin walled blood channels of the red marrow and he was able to demonstrate plugs of epithelial cells in this location He was unable to demonstrate

lymphatics in bone marrow and concluded they are absent He postulated that not only must the cancer emboli reach the marrow but the current here must be slow enough to allow the cells to grow These conditions are satisfied by the red marrow which because of its great vascularity, produces a widening of the blood stream bed with a consequent slowing of the current

The localization of bone metastases is thus explained on the basis of red bone marrow distribution In the infant all the bones contain red bone marrow, but in the adult this has been replaced by fat except in the skull sternum, ribs clavicles scapulae, vertebrae, os innominatum and the proximal portion of the extremities, where red marrow continues to persist throughout life Recent investigation by Box on a series of human jaws revealed only yellow marrow in 75 per cent In those instances in which he found small patches of red marrow he believed its presence was due to vestiges of the original red marrow or to local stimuli secondary to trauma or infection

Pinner ascribed the infrequency of metastases below the elbow and knee to the absence of red marrow in these locations He believed that bone metastases may occur occasionally by way of the lymphatics but that the principal route is hematogenous It is probable that both lymphogenous and hematogenous routes are essential to bone metastasis

Case histories are included and a list of references is appended

ALFRED O MILLER, M D

Palliative Roentgen Therapy of Bone Metastases from Breast Carcinoma L R Sante J Missouri M A 43 533-535 August 1946

The author presents 5 cases in which bone metastases from breast carcinoma were treated with roentgen rays (200 kv p 1 mm Cu and 1 mm Al filter) All the patients were women of premenopausal age and all except one had had operative removal of the breast and microscopic studies showing carcinomatous lesions of various types The metastatic lesions were mainly in the spine, pelvis femurs and skull In all cases there was a remarkable improvement with relief of pain and, in most instances healing of the areas destroyed by the metastases Several of the patients required repeated series of treatments for new metastases The author urges careful observation of these patients and prompt application of radiation to the areas showing evidence of metastasis He believes that in many instances, several years of life with freedom from pain can be added for these patients

[It has been the reviewer's experience that pain may precede by a considerable period definite roentgen demonstration of bone destruction and that it is sometimes wise to give radiation therapy even before definite roentgen evidence of metastasis is present Roentgen therapy will give considerable relief in arthritis of the spine and the dosages used while smaller than those for metastases will serve as a therapeutic test in these suspicious cases]

BERNARD S KALAJIAN, M D

Neoplasms of the Testis Oscar Auerbach Osborne A Brines and Asher Yaguda J Urol 56 368-374, September 1946

The authors report 26 cases of testicular tumor coming to autopsy in a Naval Hospital comprising 20 per

cent of all the tumor cases autopsied at this institution. What percentage this number represents of testicular tumors seen at this hospital is not stated.

The cases in this series showed no predilection for either side. In most instances the tumor was painless. The size ranged from 0.5 to 10 cm in diameter and did not determine the extent of metastatic involvement. Testicular swellings were noticed for an average of three months before a diagnosis was made. The interval between the establishment of diagnosis and death averaged eleven months and varied inversely with the duration of the disease before diagnosis.

Metastasis followed a uniform pattern in nearly all cases. Direct extension and spread along the spermatic cord were not seen. Metastasis to the retroperitoneal lymph nodes, lungs, mediastinal lymph nodes, and liver was observed in that order.

The authors give their own histologic classification of tumors of the testicle. They believe that nearly all malignant tumors of the testis are embryonal or teratoid in origin. They recognize two main groups: homologous and heterologous, which merely means that the latter plus chorionepithelioma should be labeled teratomas of varying degrees of malignancy and the remainder may be called embryonal carcinomas or seminomas. Embryonal adenocarcinoma was the most prevalent type in this series.

Treatment consisted of immediate orchiectomy and postoperative deep x-ray therapy to the chest, abdomen, and enlarged lymph nodes in the axilla and supraclavicular regions. VERA W. RITTER, M.D.

NON-NEOPLASTIC DISEASE

Irradiation of Nasopharyngeal Lymphoid Tissue: An Evaluation. Lawrence R. Boies. *Arch. Otolaryng.* 44: 129-140. August 1946.

The results of radium or radon irradiation of excessive lymphoid tissue in the nasopharynx in 73 children are discussed. *Group I:* Fifty-four patients had obvious hearing impairment and when tested showed a generalized depression of the hearing threshold through the speech frequencies and the high notes. All had had tonsils and adenoids removed and had a variable amount of nasopharyngeal lymphoid tissue with abnormal changes in the tympanic membrane. All failed to respond to the usual measures for relieving this condition. Normal hearing was recovered after irradiation in 46 of this group. *Group II:* The loss of high notes was not restored by irradiation of the tubal orifices in 4 patients with hearing loss for frequencies higher than 2048 and with a small amount of lymphoid tissue in the nasopharynx adjacent to the orifices. All of these patients gave a history of aural symptoms and recurrent infections of the upper respiratory tract. *Group III:* A group of 7 patients was treated for a hearing loss approximating the 30 decibel level or lower through the speech frequencies with a more marked loss for higher notes. It was suspected that a cochlear lesion was present in each case. Irradiation of nasopharyngeal lymphoid tissue did not produce an improvement in hearing in any of these patients. *Group IV:* Five patients with a slight loss of hearing for the speech frequencies and for high notes and a complaint of nasal obstruction were benefited by irradiation. *Group V:* Treatment was of question in 3 patients with a mucoid discharge through a chronic perforation of the drum membrane.

Keloid Formation in Both Ear Lobes. D. F. Weaver. *Arch. Otolaryng.* 44: 212-213. August 1946.

Rather large recurring keloids involving both ears developed in a Negro woman following the piercing of the lobes for the insertion of ear rings. The growths had been excised twice from one ear and once from the other. At the time of examination firm tumors one measuring $4 \times 3 \times 1.5$ cm and the other $3 \times 2 \times 2$ cm, were present. These were completely excised and roentgen therapy was given over each field (field size 2×4 cm, 150 kv, 0.25 mm Cu and 1 mm Al filtration, focal skin distance 50 cm) for a total dose of 195 r (in air). Thirty-two months later there was no evidence of recurrence of the keloids.

Twelve Years Experience in Roentgenotherapy for Chronic Arthritis. John G. Kuhns and Sidney L. Morrison. *New England J. Med.* 235: 399-405. Sept. 19, 1946.

After several years experience in the treatment of arthritis with irradiation the authors decided that a more critical analysis of the patients and their response to therapy was indicated. They therefore selected 252 patients with rheumatoid arthritis and 118 patients with osteoarthritis for treatment and study.

Each joint received 200 r in air twice weekly over two to four areas for six treatments totaling 1,200 r per field. In rheumatoid arthritis of the spine 100 r was administered to each of two areas in upper and lower every other day for twelve treatments.

Subjective evidence of change could not be relied upon but there was very little difference between the objective and subjective findings after treatment. The psychic effect of treatment did not seem to influence the results.

The best results were obtained in rheumatoid arthritis of the spine where slight improvement occurred in 34 per cent, moderate in 37 per cent, and marked in 12 per cent. Those not improved showed ankylosis and deformities. In rheumatoid arthritis without spondylitis improvement was slight in 26 per cent, moderate in 61 per cent, and marked in 35 per cent. The poorest results were in osteoarthritis where improvement was slight in 29 per cent, moderate in 40 per cent, and marked in 16 per cent.

If one course of treatment was not effective in relieving the arthritic complaint, repetition of the treatment was not indicated since it rarely produced any relief of pain. Faulty selection of patients was usually attributed as the chief cause of failure. Severe articular derangement and spur formation seemed to be a contraindication to irradiation as were also serious systemic disease and infection.

In some patients pigmentation of the skin occurred and others nausea and vomiting followed treatment and quite frequently there was an exacerbation of symptoms twelve to twenty-four hours after irradiation. Amenorrhea occurred in several patients in whom the lower spine was irradiated. Leukopenia was an occasional reaction.

Irradiation of arthritic joints seems to have a definite place in the treatment of arthritis but should not be used to the exclusion of other accepted procedures and the patients should be well selected. Follow-up films of the irradiated joints fail to show any appreciable change as a result of treatment.

JOHN B. McANENY, M.D.

Treatment of Peritendinitis Calcarea of the Shoulder Joint by Roentgen Irradiation Report of One Hundred Cases I Klein Am J Roentgenol 56 366-375 September 1946

One hundred cases of peritendinitis calcarea of the shoulder joint were divided into three groups acute (duration under a month), subacute (two months duration) and chronic (over two months) Roentgen therapy was applied anteriorly and posteriorly over a period of seven to fourteen days the treatments averaging 125 r The factors varied from 125 to 200 kv, 5 to 7 ma, 30 to 40 cm distance with a 10 by 15 cm cone Acute cases were usually given one course of treatment Subacute and chronic cases generally received more than one course The acute cases responded with improvement in seven days and 69 per cent showed partial to complete resolution of the calcification after treatment In the subacute cases, the disability period was longer, lasting an average of twenty-six days, 36 per cent of these cases showed a reduction in the calcification after treatment The chronic cases had a disability period of thirty-six days and there was reduction in the calcification in 32 per cent of this group

In those cases of peritendinitis in which calcification is bone like it is impossible to reduce it with roentgen therapy Those acute cases which showed no calcification were treated in the same manner as the other acute cases and were completely relieved As the response of the acute cases is so much more satisfactory an effort should be made to treat cases of peritendinitis calcarea as soon as possible Illustrative case histories are presented
CLARENCE E WEAVER, M D

Reticulo-Endotheliosis, with Report of Two Cases Allison E Imler Am J Roentgenol 56 343-354 September 1946

Single or multiple granulomatous lesions of bone have been variously classified as certain forms of xanthomatosis Hand-Schüller Christian's disease Letterer-Siwe's disease lipid histiocytosis lipoidosis, lipid granulomatosis eosinophilic granuloma solitary granuloma and reticulo-endotheliosis The clinical signs are dependent on the location of the granulomatous masses Headaches and localized areas of scalp tenderness are two of the most common findings Diabetes insipidus is a result of granulomatous infiltration of the hypophysis and tuber cinereum Pulmonary involvement has been frequently reported Xanthomatous infiltration may simulate a mastoiditis Exophthalmos may occur Recently it has been found that this disease is not confined to childhood

Irradiation Sickness Histamine Effect Treated with Benadryl, A Preliminary Report. J E Lofstrom and C E Nurnberger Am J Roentgenol 56 211-219 August 1946

Relief of severe symptoms of irradiation sickness in 19 cases by administration of benadryl (beta-dimethylamino-ethyl benzhydryl ether hydrochloride) is reported by the authors The complaints of anorexia, nausea, vomiting, weakness and headache were used as an index of the efficacy of the drug

For intravenous injection, 5 to 10 c.c. (50 mg to 100 mg) of benadryl was given Patients thus treated experienced a side reaction consisting of dizziness

The bone defects are not due to a disturbance of the calcium metabolism but to pressure from the granulomatous masses Most of the reported skeletal defects have been in the skull pelvis, femora, and ribs Nearly all of the fatal cases have shown extensive involvement of the lungs Diseases to be differentiated are multiple myeloma chronic osteomyelitis, cholesteatoma osteoporosis circumscripta tuberculous osteomyelitis, syphilitic osteomyelitis, and metastatic carcinoma

Satisfactory response of the bone, pituitary and pulmonary lesions can be obtained with relatively small doses of roentgen radiation None of the skull lesions in the author's reported cases received more than 400 r measured in air through any one field

It is believed that all the diseases mentioned in the first paragraph of this abstract are variants of a hyperplastic reaction of the reticulo-endothelial system and can be properly grouped under the term reticulo-endotheliosis There are insufficient data to support the claim of a lipid metabolic disorder as a primary causative factor Complete reports of two cases are given with roentgenograms showing bone involvement in the skull femur pelvis and mandible, and pulmonary infiltration and fibrosis, and illustrating response to roentgen therapy
CLARENCE E WEAVER M D

TECHNIC

A Device of Value for Roentgen Ray Epilation Oscar L Levin and Howard T Behrman Arch Dermat & Syph 54 200-201 August 1946

The authors describe, with an illustration, a device which they have found useful in centering the fields for x ray epilation for tinea capitis It consists of a flat piece of metal the size of a large treatment cone which can easily be attached to the cone by small knobs In the center of the plate is fixed a pointer of such length that when it touches an object the T S D is exactly 20 cm
JOSEPH T DANZER M D

A Note on Radiography as an Aid to Beam Direction in Radiotherapy H G Davies and M Halberstaedter Brit J Radiol 19 326-328, August 1946

The use of radiography for checking the direction of the beam in x ray therapy is advocated This is particularly useful in obese and deformed patients and when radiation must be given through a cast A kilovoltage of 110 is advocated as a suitable value A graph is given by means of which the exposure time may be determined from the thickness of the patient and the area of the field
SYDNEY J HAWLEY, M D

EFFECTS OF RADIATION

unsteady motion weakness and drowsiness lasting for one to four hours Later a general feeling of well-being developed In 7 cases benadryl was given by mouth only in the form of 50 mg capsules, one every four hours during the day These patients showed no marked side reactions, and satisfactory relief was obtained in most cases

The causes of irradiation sickness are unknown There is evidence to suggest that histamine like bodies are developed in the blood of the patient subjected to roentgen therapy, and the relief afforded by benadryl may be the result of its antihistamine action

H H WRIGHT M D

Repair of Vesicovaginal Fistula Caused by Radiation
Gray H Twombly and Victor F Marshall Surg Gynec & Obst 83 348-354 September 1946

Repair of vesicovaginal fistulas in heavily irradiated tissues is peculiarly difficult because the local blood supply is precarious, the tissues are inelastic and fixed, and are so fibrotic as to make dissection particularly of flaps, quite difficult. Also the frequent intimate association of the ureteral orifices adds to the problem. The authors of this paper are therefore particularly to be congratulated on the introduction of the method which they describe here. While the principle of repair is not original, the procedure itself is believed to be new. It is applicable in those cases of fistula where the uterus has been entirely removed or where the uterus has atrophied and the cervix has been destroyed.

The procedure is described in detail and three cases are reported in which complete success was obtained though they had been regarded as irreparable. In each instance there was resultant vaginal shortening but all the patients reported repeated successful sexual intercourse following the operation.

Repair is accomplished by using a portion of the posterior vaginal wall and by use of constant low-pressure bubble suction through a cystostomy made well away from the repair site in the dome of the bladder. The method involves a generous suprapubic cystostomy. The posterior vaginal wall is then fitted into the bladder defect by means of pressure through the rectum. The necessary area of vaginal mucosa is visualized and marked and a vaginal approach is then used. The anterior vaginal wall is then separated in its deepest portion and the posterior vaginal wall is separated in most of its deepest portion excluding the donor site. By returning to the suprapubic incision and suturing the good bladder wall to the posterior vagina (staying about 1 cm away from the ischemic scarred margin of the bladder and using loosely applied sutures) the defect is closed. By then returning to the vagina the freed anterior wall and the remaining portion of the posterior wall are united. In this fashion there are two distinct suture lines in the repair and raw surfaces are generously approximated. An important part of the treatment is the applying of constant low-pressure suction through a very high cystostomy tube thus eliminating a urethral catheter near the site of repair. It is readily apparent that if the ureter is present in the fistula its function would not be impaired. The

authors advise placing the patient in a prone position postoperatively for two weeks or more.

JAMES C KATTERJOH, M D

Controlled Nuclear Energy Its Attendant Hazards and Benefits Andrew H Dowdy Occupational Med 2 126-231 August 1946

The author considers the hazards of nuclear energy as threefold. In the first place, there are the hazards of production which are mainly those related to exposure to free radiations and dust laden with radioactive and non radioactive chemicals. The principal dangers to be anticipated from external radiation are those attributable to exposure to neutrons and gamma rays. These affect especially the blood forming organs and the reproductive cells of the ovaries and testes leading to temporary or permanent sterilization and possible effects on future offspring. The hematopoietic and reproductive systems may also suffer from the effects of internal radiation due to the inhalation, absorption, or ingestion of radioactive dusts and fission products. To these hazards is added the possible production of cancer as the result of prolonged exposure to excessive amounts of radioactive dusts.

A second danger is that incident to the use of nuclear energy as a destructive force, as in the bombings of Hiroshima and Nagasaki. In these bombings the radiation injuries in general resulted from the tremendous release of nuclear energy in the form of neutrons, gamma rays, and radioactive fission products at the moment of explosion. Radiation accounted for about 5 per cent of the fatalities in both bombings. Contrary to various reports, there was no significant or persistent induced radioactive material in and around the two cities as a result of the bomb explosion.

The great constructive possibilities of controlled nuclear energy lie in the production of radioactive and heavy isotopes for research in the basic sciences with consequent increase in the understanding of such problems as normal growth, the aging process, degenerative diseases and the pharmacology of drugs and biological products. Failure on the part of Congress to sponsor a national program directed to the utilization of controlled nuclear energy for industrial and scientific purposes and the stifling of such a program by too narrow a field of vision or too rigid security regulations constitute the third hazard mentioned by the author.

EXPERIMENTAL STUDIES

Effect of Pulmonary Resuscitative Procedures upon the Circulation as Demonstrated by the Use of Radioactive Sodium. Samuel A Thompson Edith H Qumby and Beverly C Smith Surg Gynec & Obst 83 387-391 September 1946

In pulmonary resuscitative measures one must not merely consider oxygenation of pulmonary blood but also the movement of such blood to vital centers especially when the circulation has stopped. The relative effects of various types of pulmonary resuscitation upon the circulation were determined by the use of radioactive sodium introduced into the circulation of a dog immediately after death by asphyxiation.

The sodium was made radioactive by deuterium bombardment in the cyclotron. Two cubic centimeters of normal saline containing 50 to 60 microcuries of the

sodium were injected into the femoral vein and artery after death. A Geiger Müller counter registered the movement of the blood containing the tracer. Heparin was previously injected to prevent clotting.

The methods of resuscitation were (1) double action respirator, exerting positive and negative pressure (2) suction only and (3) pressure only. Their value in producing circulation was in the same respective order in descending efficiency. The number of dogs used was small being only 7.

The authors conclude that of the methods tested alternate positive and negative pressure provides the best circulation of blood though slow. Heparin is considered of value in resuscitation by preventing clotting which would hamper or stop circulation.

ARTHUR W PRYDE M D

RADIOLOGY

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Iodinated Organic Compounds As Contrast Media for Radiographic Diagnoses

VI Experimental Studies on Emulsions of Ethyl Iodophenylundecylate (Pantopaque)¹

WILLIAM E CHALECKE, M D, GLENN E JONES, LEON L MILLER, Ph D, M D,
THEODORE B STEINHAUSEN, M D, and WILLIAM H STRAIN, Ph D

Department of Radiology, School of Medicine and Dentistry, The University of Rochester, Rochester, N Y

IN THE COURSE of the experimental work leading to the development of pantopaque (ethyl iodophenylundecylate), it was observed that stable aqueous emulsions could be obtained easily with the medium (1, 2). Study of these emulsions has shown that they have the property of coating and adhering to mucosa and that they seem well adapted to the visualization of certain body cavities. In experimental examinations in dogs and other laboratory animals the most promising results have been obtained in bronchography, although satisfactory delineation may be produced in a number of other types of examination.²

Stable emulsions of ethyl iodophenylundecylate are formed when a 50 per cent mixture by volume with water containing up to 1 per cent of a surface active agent is passed numerous times through a colloid mill or other type of homogenizer. The surface active agents studied included bile salts, various neutral soaps and a number of synthetics. Of these, oleyl methyl taurine (Igepon T gel) was found to be the most satisfactory when dissolved in

the water phase at a concentration of 0.6 per cent. On standing, the emulsion prepared with Igepon T as a surface active agent separates into a lower milky phase, containing about 70 per cent of ethyl iodophenylundecylate, and a clear upper aqueous phase. The two phases are readily redispersed on shaking, and the resulting emulsion does not settle out for some hours. The two phases are easily separated by aspiration, or the emulsion may be diluted with isotonic saline. The size of the oil droplets in the emulsion varies somewhat with the mode of preparation, but usually they are of the order of 1.5–3.5 microns. Both the 50 and the 70 per cent emulsions may be readily injected through needles and catheters of small bore.

As reported previously (2), ethyl iodophenylundecylate has a measurable toxicity in rats and mice which is consistent with the absorbability of the medium. The process of emulsification leads to an enormous increase in surface, and this in turn affects the values of the toxicity constants. The increase in surface does not

¹ Accepted for publication in December 1946. Presented in part before the Radiological Society of North America at the Thirty-second Annual Meeting, Chicago, Ill., Dec. 1–6, 1946. This work was aided by a grant from the Research Laboratories of the Eastman Kodak Co., Rochester, N. Y.

² A 50 per cent emulsion is available for investigational use from Dr. H. Sidney Newcomer, F. R. Squibb & Sons, 745 Fifth Ave., New York 22, N. Y.

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The author considers the hazards of nuclear energy as threefold. In the first place, there are the hazards of production, which are mainly those related to exposure to free radiations and dust laden with radioactive and non radioactive chemicals. The principal dangers to be anticipated from external radiation are those attributable to exposure to neutrons and gamma rays. These affect especially the blood forming organs and the reproductive cells of the ovaries and testes leading to temporary or permanent sterilization and possible effects on future offspring. The hematopoietic and reproductive systems may also suffer from the effects of internal radiation due to the inhalation, absorption, or ingestion of radioactive dusts and fission products. To these hazards is added the possible production of cancer as the result of prolonged exposure to excessive amounts of radioactive dusts.

A second danger is that incident to the use of nuclear energy as a destructive force as in the bombings of Hiroshima and Nagasaki. In these bombings the radiation injuries in general resulted from the tremendous release of nuclear energy in the form of neutrons, gamma rays and radioactive fission products at the moment of explosion. Radiation accounted for about 5 per cent of the fatalities in both bombings. Contrary to various reports, there was no significant or persistent induced radioactive material in and around the two cities as a result of the bomb explosion.

The great constructive possibilities of controlled nuclear energy lie in the production of radioactive and heavy isotopes for research in the basic sciences, with consequent increase in the understanding of such problems as normal growth, the aging process, degenerative diseases and the pharmacology of drugs and biological products. Failure on the part of Congress to sponsor a national program directed to the utilization of controlled nuclear energy for industrial and scientific purposes and the stifling of such a program by too narrow a field of vision or too rigid security regulations constitute the third hazard mentioned by the author.

EXPERIMENTAL STUDIES

Effect of Pulmonary Resuscitative Procedures upon the Circulation as Demonstrated by the Use of Radioactive Sodium Samuel A Thompson, Edith H Quimby and Beverly C Smith Surg. Gynec & Obst 83 387-391, September 1946

In pulmonary resuscitative measures one must not merely consider oxygenation of pulmonary blood but also the movement of such blood to vital centers especially when the circulation has stopped. The relative effects of various types of pulmonary resuscitation upon the circulation were determined by the use of radioactive sodium introduced into the circulation of a dog immediately after death by asphyxiation.

The sodium was made radioactive by deuterium bombardment in the cyclotron. Two cubic centimeters of normal saline containing 50 to 60 microcuries of the

sodium were injected into the femoral vein and artery after death. A Geiger Muller counter registered the movement of the blood containing the tracer. Heparin was previously injected to prevent clotting.

The methods of resuscitation were (1) double action respirator exerting positive and negative pressure (2) suction only and (3) pressure only. Their value in producing circulation was in the same respective order in descending efficiency. The number of dogs used was small being only 7.

The authors conclude that of the methods tested alternate positive and negative pressure provides the best circulation of blood though slow. Heparin is considered of value in resuscitation by preventing clotting which would hamper or stop circulation.

ARTHUR W PRIDE M D

alter significantly the LD 50 in mice as obtained by intraperitoneal injection, but does influence markedly the value found in rats. The intraperitoneal LD 50 of ethyl iodophenylundecylate has been reported to be 19 grams/kg for 24-hour kill, while that of the emulsion has been found to be of the order of 2 grams/kg. It appears, on the basis of comparative work with other species, that the rat is particularly sensitive to ethyl iodophenylundecylate. Both ethyl iodophenylundecylate and its emulsion produce the same kind of pathological changes in the liver and kidneys of rats and mice when administered at or near the lethal level.

EXPERIMENTAL STUDIES

Bronchography The spreading and coating properties of the emulsion were studied by making bronchograms in dogs. Other laboratory animals were briefly examined as experimental subjects but were found to be unsatisfactory.

By the procedure that was finally adopted, a dog, anesthetized with nembutal, was placed in a prone position on an animal table and rotated onto its left side. The table supporting the animal was then elevated 30° at the head, and 2 to 15 c c of the 70 per cent emulsion were injected under direct vision down the trachea through a small rubber tube. After two or three minutes the table was returned to a horizontal position and a series of roentgenograms was taken at intervals of five to ten minutes. Usually there was little change in the bronchogram after the first exposure. The emulsion often is seen in the smaller radicles of the bronchial system on the day following the original bronchographic study. Seven to ten days later, however, the lung fields are roentgenographically clear.

Typical bronchograms obtained by this procedure, as well as one made with the dog supine, are shown in Figure 1.

Attempts to obtain good bronchograms in anesthetized dogs with lipiodol or pantopaque proved uniformly unsatisfactory. The distribution of the media was poor.

Nebulization of pantopaque was even more unsatisfactory, perhaps because of the shallow respiration that accompanies nembutal anesthesia.

Among the 16 dogs used in the bronchographic study there was one death, due to pneumonic processes initiated by a contaminant which was identified as a type of *Vibrio*. There was no evidence in the other animals of any toxic effects. Lung sections taken from four of the dogs that were autopsied showed little, if any, change that could be attributed to the effects of the medium. This was particularly well demonstrated in a 40-lb old collie that was subjected to bronchography on four occasions at intervals of two weeks each. During the period of experimentation the dog was in excellent clinical condition. When it was killed, two weeks after the last bronchogram had been obtained, the lungs appeared darker than normal, but the gross appearance and texture were not inconsistent with the age of the animal. Microscopic sections revealed no changes that could be attributed to the use of the medium.

Retrograde Pyelography and Cystography In two experiments with dogs the peritoneum was opened, the right and left ureters were isolated, and about 2 c c of the 50 per cent emulsion were injected into each kidney under slight pressure. Roentgenograms (Fig 2) taken from these experiments show that some of the medium adheres to the wall of each kidney pelvis so that there is good to fair delineation of the calices for some time after the bulk of the medium has run out of the pelvis. Follow-up roentgenograms showed that some of the medium remains in the pelvis for several days.

Similar experiments in cystography (Fig 3) in dogs gave excellent delineation of the urethra and the bladder, with some adherence to the walls of the bladder for twenty-four hours after the examination had been completed. This was particularly noticeable with the male animals.

The findings on autopsy of the dogs used for retrograde pyelography and cystog-

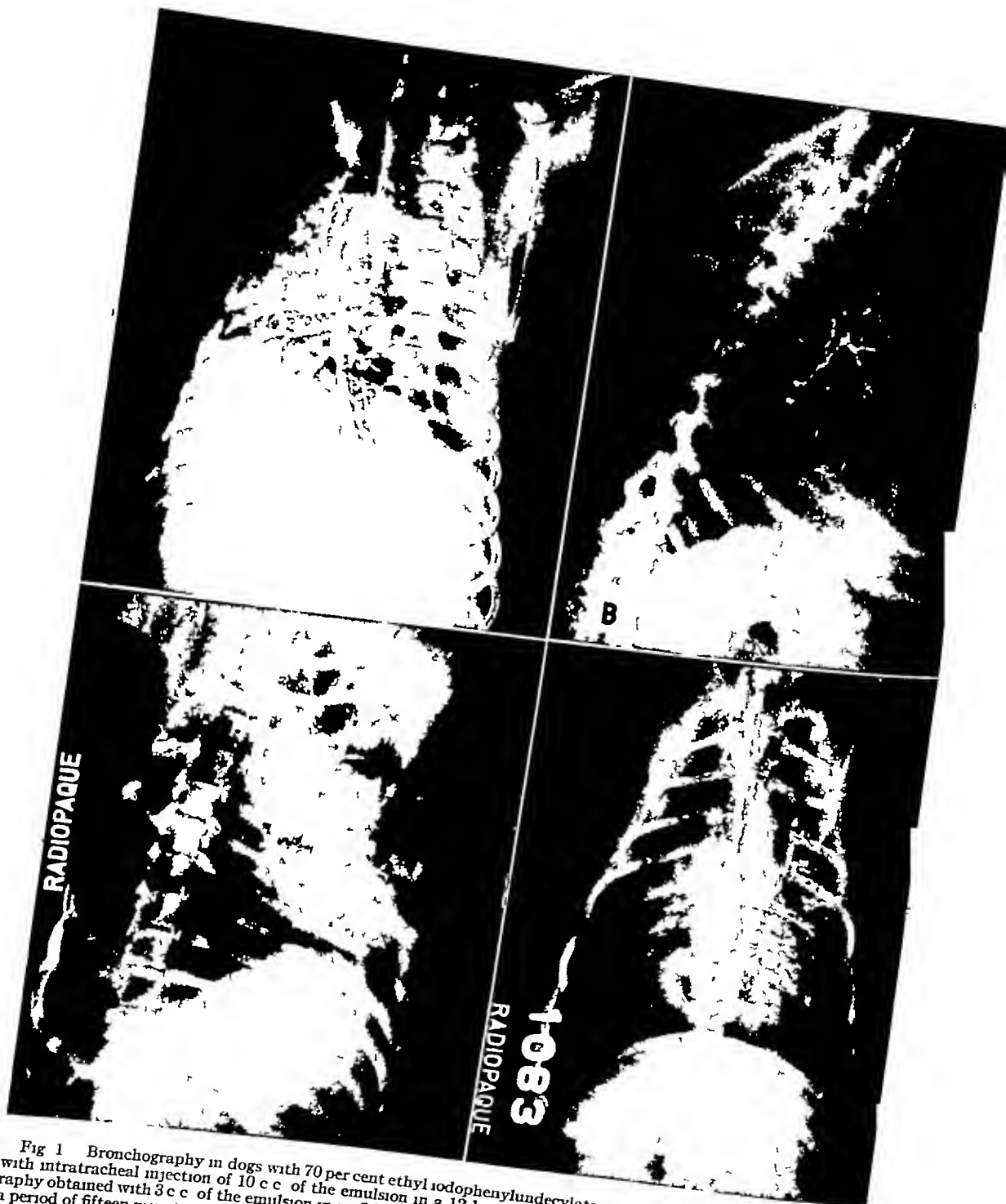


Fig 1 Bronchography in dogs with 70 per cent ethyl iodophenylundecylate emulsion. A Overfilling obtained with intratracheal injection of 10 c c of the emulsion in a 12-lb dog supine. B C and D Bronchial mucosography obtained with 3 c c of the emulsion in an 8-lb dog in a prone position. The roentgenograms were made over a period of fifteen minutes, the first view being taken ten minutes after introduction of the medium. Note that the upper lobe is uniformly filled.



Fig 3 Urethrography and cystography with 4 c c of ethyl iodophenylundecylate emulsion in a male dog. The roentgenogram, made thirty minutes after administration illustrates how a semi-opaque coating is retained for some time after the injection

fects in clinical practice. There appears to be no really satisfactory method of studying this problem in animals.

One logical application of the emulsion to clinical diagnoses appears to be in relation to problems of thoracic surgery. With the current procedures, many bronchograms made with the aid of iodized oils fail to give adequate information concerning the extent and degree of disease. In recognition of this, some work is in progress to improve the results obtained with the existing media. Thus, Fariñas (3) has developed a technic for spraying iodized oils into the bronchi in order to get surface coating. To distinguish this procedure and its results from conventional bronchography, Fariñas has introduced the term 'mucosography'. As is evident from the illustrative bronchograms obtained with dogs through the use of the 70 per cent emulsion, the coating is of a

type that reveals the details of the mucosa. It seems evident that there would be little difficulty in adapting the experimental procedure to clinical practice.

The other applications that are suggested from the animal work are not so striking, and adaptation to clinical practice may not be profitable in all fields. Nevertheless, in examinations such as cystography, urethrography, hysterosalpingography, retrograde pyelography, and cholangiography, the formation of a coating that will remain for some time may reveal additional information.

In addition to the emulsion proposed in this paper, there are a number of emulsions of iodized oils that have received study both experimentally and clinically. Emulsions prepared from water-acacia mixtures with campidol (4) or iodochlorol have been available for retrograde pyelography for some years but have not attained

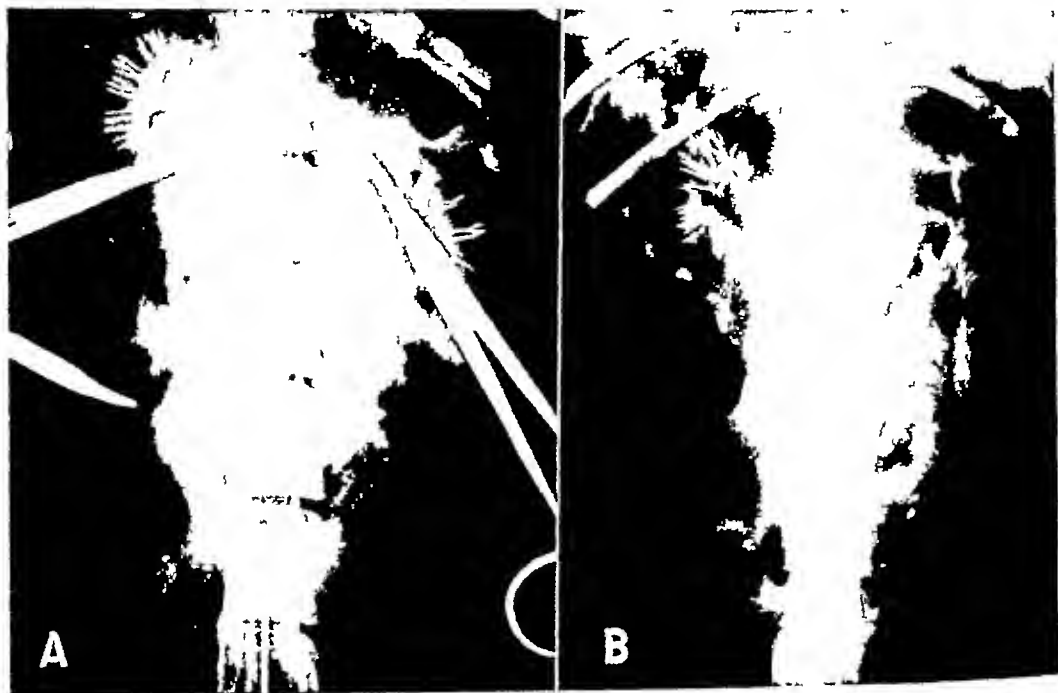


Fig 2 Visualization with ethyl iodophenylundecylate emulsion of the renal pelvis of a dog. A Delineation obtained in the right kidney immediately and in the left kidney twenty minutes after injection. B This film taken thirty minutes after A shows the residual coating on the calices after the bulk of the medium had run out.

raphy were unremarkable both grossly and microscopically.

Hysterosalpingography The uteri of two dogs and three rabbits were exposed by laparotomies. The proximal ends of the uteri were clamped off, and an attempt was made to force the 50 per cent emulsion through the fallopian tubes. In every instance this was unsuccessful. After roentgenograms were made, the clamps were removed and the animals closed up. Subsequent roentgenograms showed that the medium remained in the uterine passages for several hours. There were no obvious disturbances in the behavior of the animals subsequently. One of the dogs was killed after eighteen days, and the other bred. The uterine passages were found to be normal in the case of the sacrificed animal, and were assumed to be functioning properly when the second dog was delivered in due course of a litter of 5 pups.

Cholangiography Roentgenograms made following injection of the hepatic tree operatively exposed in dogs, rabbits, and rats, showed that the opacity of the 50 per

cent medium was adequate for the delineation of small ducts. Two dogs were carried along after operation, and sections were made of the liver. There was no evidence of damage.

Intravenous Injections The early preparations of the 50 per cent emulsion could not be injected intravenously with any safety, but as the technique of preparing the emulsion was improved it was found that amounts up to 1 cc/kg could be injected into the saphenous veins of dogs without immediate or subsequent effects. No attempt was made to determine the lethal dose, however. In rabbits, injections of 0.5 cc/kg in a marginal ear vein produced no early or late EKG changes.

DISCUSSION

The experimental work shows that the 50 per cent emulsion of ethyl iodophenylundecylate prepared with the aid of oleyl methyl taurine is non-toxic in the regions and at the concentrations studied. The animal experiments are not relevant as to the production of transient irritating ef-



Fig 3 Urethrography and cystography with 4 c.c. of ethyl iodophenylundecylate emulsion in a male dog. The roentgenogram made thirty minutes after administration, illustrates how a semi-opaque coating is retained for some time after the injection.

fects in clinical practice. There appears to be no really satisfactory method of studying this problem in animals.

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The other applications that are suggested from the animal work are not so striking, and adaptation to clinical practice may not be profitable in all fields. Nevertheless, in examinations such as cystography, urethrography, hysterosalpingography, retrograde pyelography, and cholangiography, the formation of a coating that will remain for some time may reveal additional information.

In addition to the emulsion proposed in this paper, there are a number of emulsions of iodized oils that have received study both experimentally and clinically. Emulsions prepared from water-acacia mixtures with campidol (4) or iodochlorol have been available for retrograde pyelography for some years but have not attained

wide use. This is due in part to the fact that their viscosity is relatively high, and usually it has been necessary to inject them from a syringe rather than by a gravity method.

In 1938 a very interesting 50 per cent emulsion of ethyl triiodostearate, prepared and stabilized with the aid of lecithin and gelatin, was introduced in Germany under the name Jodsol for hepatosplenography (5, 6, 7). Since then Jodsol has been studied for angiography (8) and phlebography (9) but it is still partially in the experimental stage. Apparently the medium must be stored under refrigeration to prevent the oil particles from coalescing, and this is obviously a great disadvantage. In clinical use, up to 80 cc are injected intravenously, and adequate shadows of the blood vessels are obtained if the iodine concentration is 20 per cent or more.

It is uncertain whether the presently described emulsion of ethyl iodophenylundecylate is suitable for intravenous work. More experimental studies will have to be done before it can be considered for this type of application. Nevertheless, the particle size of the droplets is of the correct magnitude and the emulsion does not break down when stored for long periods of time at room temperature.

SUMMARY

Experimental studies in dogs and other laboratory animals show that emulsions of

ethyl iodophenylundecylate (pantopaque) and water, prepared with the aid of 0.6 per cent of the surface active compound oleyl methyl taurine, have the property of coating and adhering to mucosal surfaces. The application of a 70 per cent medium to bronchography, and of a 50 per cent medium to a variety of other diagnostic problems, is illustrated by experimental work in dogs.

260 Crittenden Blvd
Rochester 7 N Y

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SUMARIO

Las Emulsiones de Yodofenilundecilato de Etilo como Medios de Contraste

Los estudios experimentales en perros y otros animales de laboratorio muestran que las emulsiones de yodofenilundecilato de etilo (Pantopaco) y agua, preparadas con la ayuda de 0.6 por ciento del compuesto activo superficial, oleilo-metilo-aurina, poseen la propiedad de recubrir las

superficies de las mucosas, adhiriéndose a las mismas. La aplicación de un medio de 70 por ciento a la broncografía y de un medio de 50 por ciento a otros varios problemas de diagnóstico queda demostrada por la experimentación en perros.

Iodinated Organic Compounds As Contrast Media for Radiographic Diagnoses

VII Visualization of Empyema Cavities with the Aid of Ethyl Iodophenylundecylate Emulsion¹

MURRAY P. GEORGE, M.D., EARLE B. MAHONEY, M.D., HERMAN E. PEARSE, M.D., and
WILLIAM H. STRAIN, Ph.D.

Departments of Radiology and Surgery, School of Medicine and Dentistry and Strong Memorial Hospital, The University of Rochester, Rochester, N. Y.

VISUALIZATION of a group of eight empyema cavities has offered opportunities to test clinically the properties of the emulsion of ethyl iodophenylundecylate² described in the preceding paper (1). As brought out in that paper, the emulsion has the property of coating and adhering to tissue surfaces to a rather high degree. This has led to a more perfect delineation of the cavities and of the response of the abscesses to chemotherapy and/or surgery.

The emulsion used was one containing 50 per cent of ethyl iodophenylundecylate, corresponding to an iodine content of 15 per cent. In every instance visualization was satisfactory both fluoroscopically and roentgenographically. After injection of the medium into each cavity, it was washed out by saline lavage. Relatively small amounts of the medium were required for visualization in each instance, and the injection and lavage were carried out with a minimum of discomfort to the patient. In none of the cases was there evidence of toxic reactions of any sort.

ILLUSTRATIVE CASES

Eight empyema cavities were visualized with the aid of ethyl iodophenylundecylate emulsion. Of these, 7 were closed and 1 was open. Three of the cases are presented in some detail to illustrate the ease of use of the medium and the adequacy of the visualization.

CASE I J. F., a 52-year-old woman, had had repeated bilateral pleural effusions for a period of eighteen years. She was subjected to numerous examinations, including lipiodol bronchography. Several years prior to this admission, the fluid in the left pleural space became infected (*Staphylococcus aureus* and anaerobic streptococcus), and a chronic empyema resulted. The cavity was drained over a period of months, during which time it was visualized three times with lipiodol. Fifteen months after a left rib resection, the cavity failed to heal spontaneously, and in order to visualize it prior to thoracoplasty, about 20 c.c. of 50 per cent ethyl iodophenylundecylate emulsion were injected (Fig. 1). Following the examination, the emulsion was washed out with saline lavage. With the patient in the prone position it was possible to inject 63 c.c. of saline into the cavity. An injection of ethyl iodophenylundecylate emulsion eleven days post-operatively showed obliteration of the cavity but demonstrated a small draining sinus. The latter was healed completely ten days after discharge.

Comparison of the visualization achieved with the emulsion of ethyl iodophenylundecylate in this case with that obtained with the iodized oil was strikingly in favor of the emulsion. Small amounts of residual oil from the early examinations had been present in the tissues for some years, and these droplets interfered with an appraisal of whether small amounts of the emulsion remained after the examination. Apparently after each examination all the emulsion was removed by the saline lavage.

CASE II G. Q., a 64-year-old woman, had had pneumonia three times in the past. Although prior to this admission her local physician had been treating her with sulfamerazine, she was admitted

¹ Accepted for publication in December 1946. Presented in part before the Radiological Society of North America at the Thirty-second Annual Meeting, Chicago, Ill., Dec. 1-6, 1946. This work was aided by a grant from the Research Laboratories of the Eastman Kodak Co., Rochester, N. Y.

² Ethyl iodophenylundecylate emulsion is available for investigational purposes from Dr. H. Sidney Newcomer, I. R. Squibb & Sons, 745 11th Ave., New York 22, N. Y.

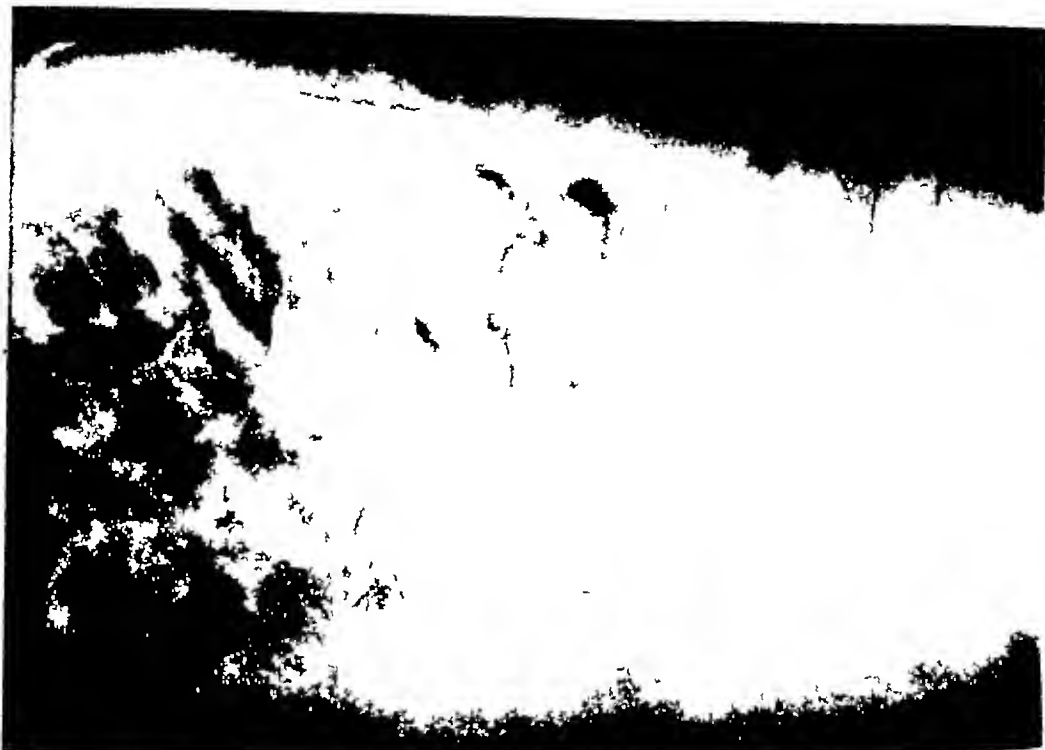


Fig 1 Case I Visualization of a 63 cc open empyema cavity with 20 cc of ethyl iodophenylundecylate emulsion, illustrating how the medium coats all parts of the cavity



Fig 2 Case II Visualization of a closed empyema cavity by injection of ethyl iodophenylundecylate emulsion. The presence of a coagulum of pus inhibits the distribution of the medium to some extent

to the hospital because her condition was unimproved. On the day of her admission she was acutely ill and her disease continued to run an acute and toxic febrile course. At no time was a pneumococcus grown from the sputum, but *Streptococcus hemolyticus* was isolated from the fluid aspirated by thoracentesis. Treatment consisted in a combination of chemotherapy and thoracenteses. Following thoracentesis on the 33rd hospital day, ethyl iodophenylundecylate emulsion was injected through the needle into the empyema cavity to determine its size and to ascertain whether surgery was indicated at this time. On the following day a trocar was inserted and a catheter passed into the cavity. Within a few days after the catheter was inserted, the temperature returned to normal. A later visualization on the 84th day, satisfactorily delineated a cavity much decreased in size. The patient was discharged from the hospital on her 107th day.

The visualization of the cavity on the 33rd day is shown in Figure 2. The delineation of the upper part of the cavity is inadequate, due to the use of too little medium. The patient was so acutely ill that it was inadvisable to repeat the examination with more of the contrast agent.

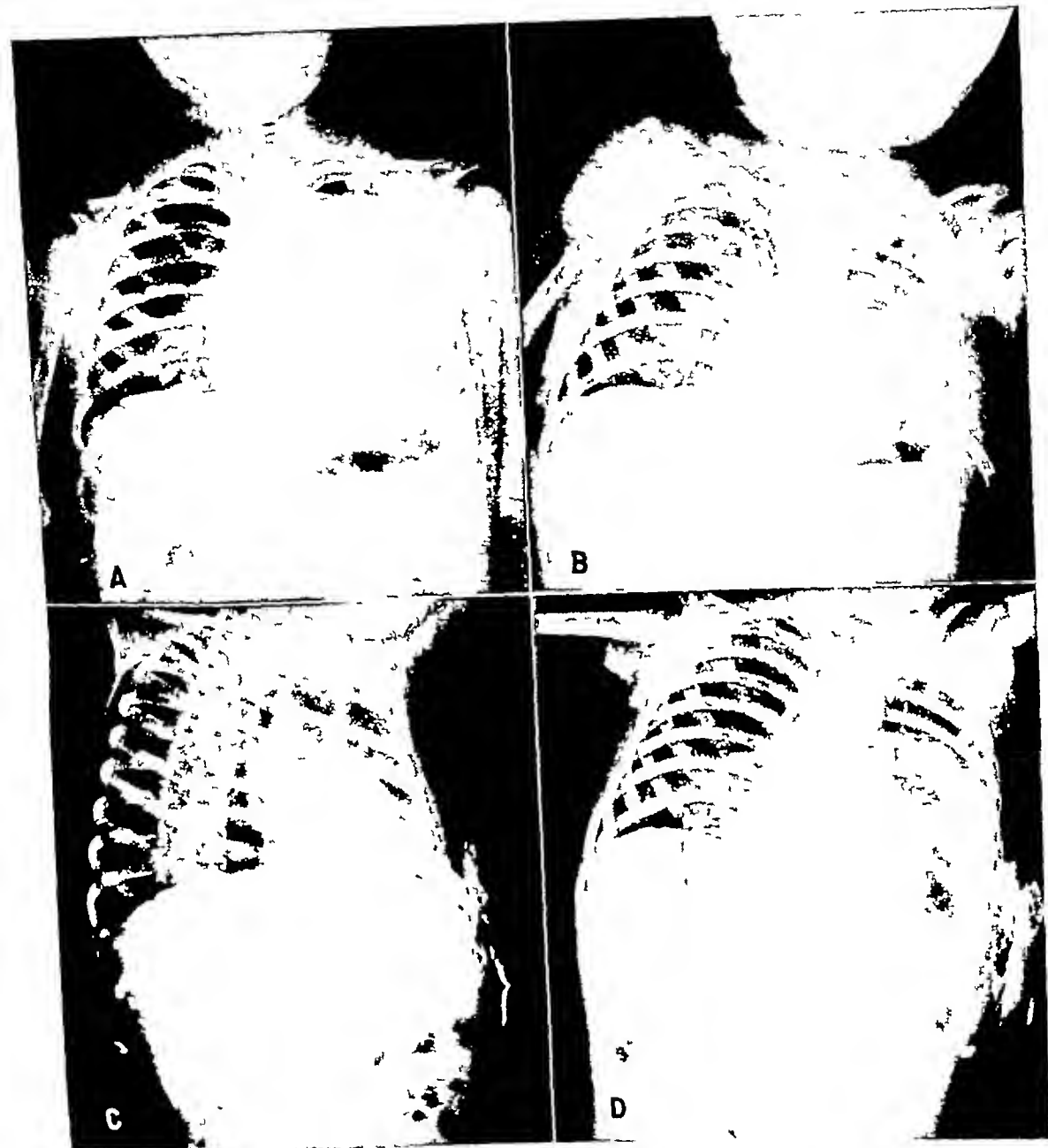


Fig 3 Case III Visualization of an empyema cavity by injection of ethyl iodophenylundecylate emulsion through a drainage tube A Condition of the chest three days after admission B Position of the catheter inserted on the 28th day C and D Visualization of the cavity following the injection of 10 c.c. of ethyl iodophenylundecylate emulsion through the catheter on the 35th day See also Fig 3 E and F

The roentgenogram shows that a considerable portion of the emulsion is collected about a coagulum of pus. It is possible that injection of saline might have given a more uniform distribution of opacity. In subsequent procedures the ethyl iodophenylundecylate emulsion was removed

by saline lavage, and at the time of discharge the chest was free of shadows due to radiopaque medium.

CASE III D K, a 20 month-old girl, was admitted because of abdominal pain following an upper respiratory infection of a week's duration. X-ray examination on the day of admission confirmed the



Fig 1 Case I Visualization of a 63 c.c. open empyema cavity with 20 c.c. of ethyl iodophenylundecylate emulsion illustrating how the medium coats all parts of the cavity



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iodized oils, Gordon (2) in 1944 employed nebulized 35 per cent diodrast or skiodan-acacia mixtures in open empyema cavities. This procedure has the advantage that after the examination all the contrast medium is absorbed, but suffers from the disadvantage that no technic has been developed for its use in closed cavities.

Since the advent of sulfa drugs and penicillin, empyema cavities are seen less frequently, and the treatment has become far more satisfactory. When a cavity does form, however, it is desirable to visualize it completely and to follow the course of corrective measures. As Blades (3) has emphasized, the cavity cannot be considered cured until it has been obliterated.

SUMMARY

The delineation of empyema cavities through the use of ethyl iodophenylundecylate emulsion has been described in detail. The medium is easily injected, distributes itself without posturing of the patient, and is readily removed by saline lavage. Where a coagulum of pus is not present, the medium distributes itself on the walls of the cavity so that double contrast studies are obtained.

260 Crittenden Blvd
Rochester 7 N Y

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DISCUSSION

Sydney F Thomas, M D (Palo Alto, Calif) These papers are quite revealing. Mucosal studies of the trachea are something we haven't seen before and to which we are going to have to pay more attention. Mucosal studies of the urinary tract are also going to call for greater attention because, while air contrast pyelograms have been used, they are not exactly satisfactory in the presence of non-

opaque stones. This new medium should find some usefulness there.

The spreading and coating qualities of the medium are its main advantages, but another thing about it that is remarkable to me is that in one or two of Dr Strain's cases it was completely gone at the time of the patient's discharge from the hospital. In other words, it doesn't stay in the alveoli like lipiodol and confuse one's view of the chest for months.

If anyone would raise the objection that there is a possibility of the emulsion getting into the blood vessels, Dr Strain has already stated that they have given this material intravenously with no significant toxicity and with no electrocardiographic changes, therefore probably no embolism.

We started attacking this problem in about 1942. We did it in a little different way but were not as successful in getting a uniform emulsion with a particle size as small as Dr Strain has produced. We had no new medium, and we used lipiodol, emulsified it, and gave it intravenously. We are interested in hepatosplenography, but there is one other use that should be mentioned—placentography. I believe we are eventually going to be able to visualize the placenta—a reticulo endothelial organ, like the spleen and liver. There should be many other uses for this method other than those which have been mentioned here. As far as sinus tracts are concerned, I think this really is a step ahead.

William H Strain, Ph D (closing) I shall close by supplementing my earlier remarks a bit. We have used the emulsion for cholangiograms a number of times, and have done two hysterosalpingograms with it, I believe. Dr Golden became interested in the medium, and at his suggestion a study was sent to Dr C L Buxton at Presbyterian Hospital in New York City. There the medium was used in some eight or nine cases for the visualization of the fallopian tubes. At Presbyterian the examination is called uterotubography, an expression which I prefer. In each case Dr Buxton reported a fair amount of reaction, but we obtained no adverse comments from the patients examined at Strong Memorial by Dr George Heckel. In our cases the tubes were not patent, and I understand from a telephone conversation with Dr Buxton that in all his cases the tubes were patent. Obviously the medium requires much further clinical study, and those of you who are interested may obtain some from Dr H S Newcomer of E R Squibb & Sons.

I suspect that for some time the emulsion will be rather difficult to get. The preparation is dependent on the supply of ethyl iodophenylundecylate (pantopaque), and this in turn is dependent on the availability of undecylenic acid. As I understand the commercial situation, the supply of this acid is currently short due to lack of adequate stocks of castor oil and the competitive use of undecylenic acid in preparations for the treatment of athletes foot.



Fig 3 E Re examination on the 47th day F Chest film 90 days after admission The series shows the course and the progressive obliteration of an empyema cavity The effectiveness of lavage in removing the emulsion is evident from these views

diagnosis of bronchopneumonia in the lower lobe of the left lung, and sulfadiazine therapy was started. By the third hospital day there was clinical and roentgenographic evidence of a left hydrothorax, and culture of fluid obtained by thoracentesis yielded *Staphylococcus aureus hemolyticus*. On the fifth hospital day the thoracentesis was repeated, *Staphylococcus aureus hemolyticus* was again isolated, and administration of penicillin was started both intrathoracically and systemically. On the 15th day of the illness a trocar was inserted to permit drainage of the cavity. Following the insertion of a larger catheter on the 25th hospital day the patient was somewhat improved and by the 35th day was having minimal drainage from the cavity. At that time about 10 c.c. of ethyl iodophenylundecylate emulsion were introduced through the catheter to outline the cavity and to ascertain whether further surgery was required. Since only a small cavity was outlined, it was felt that there was no indication for immediate surgery, but that the patient should be followed clinically and by repeated radiopaque visualization. The catheter was left in place and chemotherapy was continued. For the next twelve days the course was relatively afebrile and asymptomatic. Examination of the cavity with ethyl iodophenylundecylate emulsion was then repeated. The cavity was found to be considerably smaller, so the patient was discharged to her home on the 55th day, and was followed in the clinic thereafter.

The course of *empyema thoracis* in this patient is illustrated in detail in Figure 3, to show the value of the emulsion of ethyl iodophenylundecylate in following the ob-

literation of the cavity, and the completeness with which the medium may be removed by saline lavage.

DISCUSSION

Through the use of the emulsion of ethyl iodophenylundecylate the visualization of empyema cavities is much simpler and more complete than by conventional methods. After introduction either directly or through a drainage tube, the medium is distributed by the normal respiratory movements to all parts of the cavity. The presence of a coagulum of pus is a handicap, however, and the medium collects to a certain degree on the surface of the coagulum. This does not appear to interfere with the delineation of the extent of the cavity and from some aspects is helpful. When the examination has been completed, the medium may be removed almost completely by saline lavage and any small residuum appears to be absorbed in a few days.

Visualization of empyema cavities is usually conducted with iodized oils. Although the procedure is essentially simple, it is often difficult to obtain good distribution of the oil, and it is frequently hard to remove it all at the end of examination. In an attempt to improve on the use of

Iodinated Organic Compounds

As Contrast Media for Radiographic Diagnoses

VIII Studies on Tetraiodophthalimidoethanol as a Medium for Gastro-Intestinal Visualization¹

GLENN E JONES, WILLIAM E CHALECKE, M D, JOSEPH DEC, Ph D, JOHN A SCHILLING, M D,
GEORGE H RAMSEY, M D, HAROLD D ROBERTSON, and WILLIAM H STRAIN, Ph D

Departments of Radiology and Surgery, School of Medicine and Dentistry and Strong Memorial Hospital, The University of Rochester, Rochester, N Y

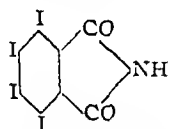
APPARENTLY NO serious attempt has been made to utilize iodinated organic compounds for the visualization of the gastro-intestinal tract. Iodized oils are used to a limited extent for specialized examinations, and there are occasional reports of experimental attempts to employ other iodinated compounds.

To evaluate the possibilities of particulate iodinated organic compounds for gastro-intestinal work, tetraiodophthalimide (I), tetraiodophthalimidomethane (II), and tetraiodophthalimidoethanol (III) were synthesized and studied experi-

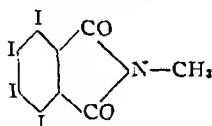
mentally in dogs and to a limited extent clinically. It was soon apparent that the parent compound, tetraiodophthalimide, produced increased motility of the stomach. Although this effect may be useful for certain specialized problems, it does not appear to be a desirable quality for general use. Attention was then turned to tetraiodophthalimidoethanol. After some study it was found that this medium, when ground in water to a particle size of 1 to 2 microns, formed a suspension that had a number of desirable qualities. In comparison with barium sulfate suspensions, tetraiodophthalimidoethanol suspensions do not settle out as readily, are not so gritty, delineate more completely experimentally produced gastric lesions, adhere better to the bowel wall, and apparently do not inspissate so readily.

Tetraiodophthalimidoethanol is a light yellow solid with a slightly greenish cast. The medium contains 73 per cent iodine and is considerably more opaque to x-rays than barium sulfate. The preparation of suitable aqueous suspensions on an experimental scale is a time-consuming process, since the product of chemical synthesis must be micronized in the dry state and then ground in a ball mill with water for several weeks. A properly prepared suspension is essentially non-settling at concentrations above 15 per cent by weight and becomes very thick at concentrations above 30 per cent.

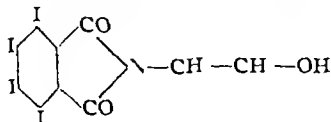
Studies on toxicity are still somewhat incomplete, but it appears that tetraiodophthalimidoethanol is of about the same order of toxicity as barium sulfate. Oral administration to fasting rats in doses up to 15 grams/kg produced no toxic symptoms. Intraperitoneal injections in mice



I Tetraiodophthalimide



II Tetraiodophthalimidomethane



III Tetraiodophthalimidoethanol

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SUMARIO

El Yodofenilundecilato de Etilo en la Visualización de las Cavidades Empiémáticas

Mediante la inyección de una emulsión de yodofenilundecilato de etilo (véase el trabajo anterior) se obtuvo la visualización roentgenoscópica y roentgenográfica de las cavidades empiémáticas. El medio se inyecta fácilmente, se esparce sin que haya que cambiar la posición del enfermo y se

extrae fácilmente por medio del lavado con solución salina. Si no hay coágulo de pus presente, el medio se reparte por las paredes de la cavidad, de modo que se logran estudios de doble contraste. Tres de los 8 casos en que se utilizó el procedimiento son descritos.



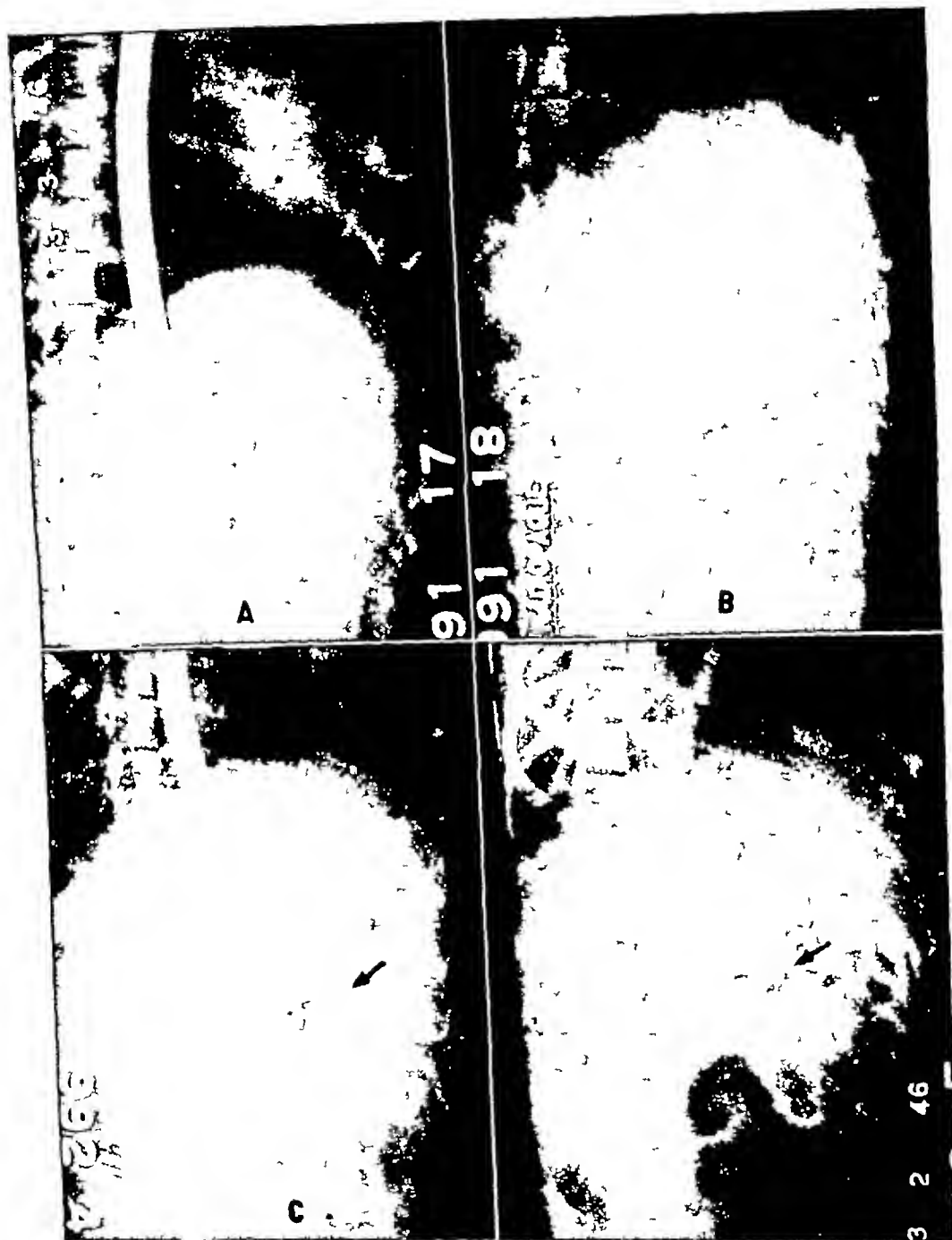


Fig 2 Comparative visualization with barium sulfate and tetraiodophthalimidoethanol of a marginal ulcer in the stomach of a dog. A and B show the distribution of barium sulfate. A being taken immediately after administration and B after twenty minutes. C and D show the delineation of the ulcer with tetraiodophthalimidoethanol, C being the view on administration and D the delineation after twenty minutes.

miosis is visualized in the examination conducted with tetraiodophthalimidoethanol, but not in the one with barium sulfate.

The technique of the examination was varied somewhat with each animal. First each dog was anesthetized with nembutal



Fig 1 Photograph of a dog's stomach showing the site and type of marginal ulcer (arrow) produced by histamine beeswax injections after gastrojejunostomy. In the illustration the esophagus is at the top, the afferent loop is on the left, and the efferent loop on the right

were productive of toxic manifestations at the range of 7.5 to 10 grams/kg. In comparison, barium sulfate suspensions when injected intraperitoneally in mice produced similar but less severe reactions at the same level of 7.5 to 10 grams/kg. Growth curves of rats raised on diets containing 4 per cent of added tetraiodophthalimidoethanol were more nearly normal than those obtained with 4 per cent added barium sulfate, but this may be due entirely to the effect of particle size, since the tetraiodophthalimidoethanol averaged about 10 microns, and the barium sulfate 1 to 2 microns.

EXPERIMENTAL STUDIES

Preparation of Suspensions Tetraiodophthalimidoethanol as obtained by synthesis consisted of needles varying in particle size from 3 to 25 microns. Suitable suspensions with a particle size of 1 to 2 microns were prepared from the stock material either by wet ball-milling with water for ten to twelve weeks or by wet ball-milling of a micronized product for two to three weeks. The ball-milling

was done in a 1-gallon apparatus using charges of about 2 kg, of which usually 25 per cent was the iodinated medium. Periods of ball-milling shorter than those specified were inadequate to reduce the particle size uniformly to 1.5 to 2 microns.

Commercial barium sulfate was found to have a particle size of 1.5 to 3 microns, and to be fairly uniform in composition. By micronizing or by wet ball-milling, the size of the particles could be reduced to 1 to 2 microns, and the uniformity could be improved slightly. Suspensions were prepared either by wet grinding or by following the clinical practice of stirring barium sulfate with water mechanically. For some of the work, gelatin (1) or starch was added to give better suspensions.

Gastro-Intestinal Series in Dogs Initially the iodinated medium was compared with barium sulfate suspensions by studying the delineation of the rugal pattern in normal dogs. Although the iodinated medium uniformly gave more satisfactory visualization of the rugae, it was felt that the experimental test was not critical enough. A much more satisfactory test object was found in dogs in which marginal stomach ulcers had been produced by the general technique developed by Code and Varco (2). In such dogs an ulcer is produced by intramuscular injections of histamine-beeswax following various types of gastrojejunostomy. The anatomical relationships that are produced are illustrated by the photograph (Fig 1) of a stomach of one of the dogs used in the work. Comparative studies were made with barium sulfate suspensions and with tetraiodophthalimidoethanol suspensions in 4 such dogs. In 3 dogs an ulcer or stomach lesion was demonstrated with the iodinated medium, but in only one of these was the stomach lesion delineated when barium sulfate was used. In the fourth dog no lesion could be demonstrated either with the iodinated medium or with barium sulfate and none was found on autopsy. The comparison of the two media in one dog is shown in Fig 2, in which a filling defect at the line of anasto-

and placed in a supine position. By means of a stomach tube, a dose of 50-70 c c of the suspension of the contrast medium under study was then given. A series of roentgenograms was then made at intervals during the first thirty minutes with the animal in various positions. As a variant, the dog was placed in an upright position with the hindquarters supported by a sling.² No one position was uniformly satisfactory, but with each dog there was usually an ideal position.

Because of the extensive alterations in the arrangement of the intestines as a result of the operative intervention, roentgenograms taken more than thirty minutes after the administration of the medium were difficult to interpret.

To study the inspissating characteristics of tetraiodophthalimidoethanol, the feces of dogs fed with the medium were compared with those given barium sulfate. Almost uniformly the consistency of the feces was much softer when the iodinated medium was used. An extended experiment was carried out with a 10-kg dog that was to be sacrificed in connection with another problem. This animal received two doses daily of 19 grams of tetraiodophthalimidoethanol for a period of eight days. At autopsy the entire digestive tract was found to be filled with varying amounts of the yellow tetraiodophthalimidoethanol, and the consistency was found to become progressively harder as the rectum was approached. Both grossly and microscopically the tissue of the digestive tract was unremarkable.

Opaque Enemas in Dogs The procedure for the visualization of the large bowel of the dog was varied from time to time, but the following technic is typical of the method giving the most uniform results.

The dog was anesthetized with nembutal, placed in a supine position, and given a tepid enema of isotonic saline. Usually from 3 to 5 liters of saline were necessary to clear the large intestine of all feces. About an hour after the saline enema was

completed, the dog was given an enema of the radiopaque medium under consideration. Nembutal markedly relaxes the anal sphincter, and it was impossible for the dog to retain the enema without the use of a Foley catheter. Even with this device, retention was often difficult because the catheter would slip out over the smooth mucosal surface. After a waiting period of fifteen minutes, corresponding to the time involved clinically in fluoroscopy, the medium was expressed by gentle palpation of the abdomen, and the large intestine was insufflated through the Foley tube with 70 to 100 c c of air. Routine anteroposterior and lateral films were taken after each step in the procedure. Following the examination, the dog was rested for four to seven days before the procedure was repeated with the same or another radiopaque medium.

To appraise the adherence of each medium to the mucosal surfaces, it was necessary to take both anteroposterior and lateral films after the air insufflation. Thus the coating on all surfaces of the bowel wall could be studied (Fig 3). The roentgenograms were then graded to evaluate the comparative excellence of the delineation of the bowel wall with the various suspensions.

For an examination to be considered "excellent," 75 per cent or more of the bowel wall in both views had to be covered with a uniform thin coating of the medium. Roughly half of the bowel had to be coated if the examination was to be rated as "good." An examination was considered "fair" if less than 50 per cent of the bowel wall was delineated. Variable results were obtained in the "poor" examinations. In most of them little if any of the mucosal surface was covered with medium, while in some series the medium had settled out of suspension onto the dependent bowel wall. Table I summarizes the 33 examinations which were done, using 6 dogs. The data on barium sulfate include the results obtained with U S P barium sulfate, I-X barium sulfate, barium sulfate and starch, and barium sulfate and gelatin

²The authors are indebted to Dr. Ross Golden for the suggestion that this position be employed.

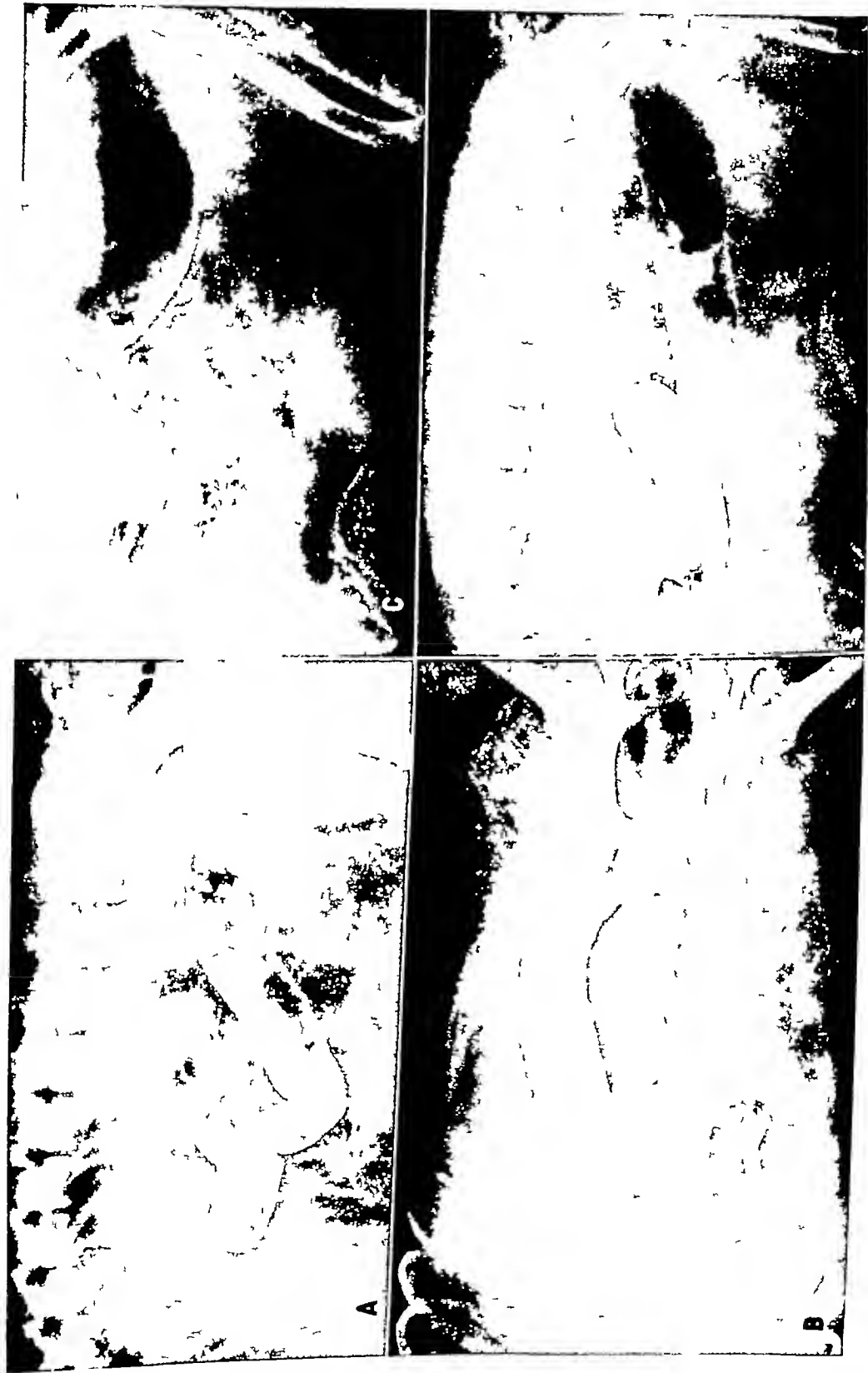


Fig 3 Double contrast studies of the bowel of the same dog comparing the adherence of tetradiophthalimidoethanol and barium sulfate. A and B made with tetradiophthalimidoethanol show uniform coating both in the internit and anteroposterior views. Studies with barium sulfate are shown in C where the coating is very poor and D where the medium has settled to the dependent portion of the bowel to give a fair coating.

icity studies on a medium advocated for use in gastro-intestinal work should include a consideration of the response of animal tissues to the preparation in the digestive tract, in the peritoneal cavity, and in the lower respiratory tract. The studies on tetraiodophthalimidoethanol have been quite complete with respect to the digestive tract, moderately complete with regard to the peritoneal cavity, and inadequate in relation to the respiratory system. The information available from the animal studies is adequate for clinical appraisal in selected cases, however, but should be supplemented by further observations if the medium proves promising in clinical applications. Many problems are difficult to solve satisfactorily. In illustration, there may be cited the question of whether it is safe to use barium sulfate in infants, where there is the possibility that some of the medium may on occasion be aspirated into the respiratory tract. The relatively rare occurrence of barium sulfate entering the peritoneal cavity through perforation of an ulcer has raised similar questions. From a practical point of view, the damage to the system resulting from such peritoneal escape appears to be tolerable (3).

At the outset of the work, it was felt that the property of remaining in suspension was the most important aspect of a radiopaque medium designed for use in gastro-intestinal work. The many admixtures that are made with barium sulfate to accomplish this purpose naturally influenced this point of view. As the work progressed, it became apparent that adherence to the gastric mucosa was of equal, if not greater, importance, if progress were to be made in increasing the accuracy of the gastro-intestinal series or of the opaque enema study. It is quite apparent from the results of the oral administration of barium sulfate and of tetraiodophthalimidoethanol to dogs with stomach lesions that the accuracy of the delineation was much greater with the iodinated medium than with the standard barium sulfate.

With the opaque enemas the double contrast studies were uniformly better with tetraiodophthalimidoethanol than with barium sulfate. Surprisingly, the incorporation of additives with barium sulfate appeared to decrease the adherence of the medium to the bowel wall. This was not always apparent when anteroposterior views alone were taken, but became evident only when both lateral and anteroposterior exposures were made.

Although experimentally the iodinated medium is superior to barium sulfate in that it does not settle out as readily, adheres better to the bowel wall, and apparently does not inspissate as readily, it remains to be shown that these advantages make for more accurate interpretations in normal clinical practice. From the limited clinical experience that is now available, it can be said only that suspensions of tetraiodophthalimidoethanol are more palatable than barium sulfate and appear to be free of toxic reactions. Before a large scale clinical trial can be considered, it must be shown that an iodinated organic compound, one that will be relatively expensive, will give enough information to justify the cost. Work is under way to make a critical comparison clinically of such new media in selected cases.

SUMMARY

Comparative studies in dogs of barium sulfate suspensions and of tetraiodophthalimidoethanol suspensions show that the iodinated medium gives more complete and more accurate delineation of experimentally produced stomach lesions. Double contrast enema studies in dogs were similarly much more satisfactory with the iodinated organic medium than with barium sulfate. A limited clinical experience with tetraiodophthalimidoethanol has shown that the new medium is more palatable than barium sulfate, and apparently as safe to use. Further use of the new medium is dependent on the outcome of critical comparisons with barium sulfate in selected clinical cases.

TABLE 1 COMPARISON OF DOUBLE CONTRAST BOWEL STUDIES

Medium	Tetraiodophthalimidoethanol				Barium Sulfate			
	Excellent	Good	Fair	Poor	Excellent	Good	Fair	Poor
Dog 1	2	1						
2	1					2	2	3
3					1		1	1
4		2				2		1
5		1		1		1	1	3
6	1					1		1
		1		1				2
Total	4	5	0	2				
Per cent	36	46	0	18	1	6	4	11
					5	27	18	50

according to the formula published by Abel (1). In passing, it may be noted that most of the modified barium sulfate formulas were less satisfactory than barium sulfate *per se*.

CLINICAL STUDIES

In all, 56 oral examinations and 4 opaque enema studies were carried out clinically with the suspensions of tetraiodophthalimidoethanol. Many of the early examinations were made with suspensions in which the particle size was of the order of 3.5 to 8 microns, and the findings were not remarkable. It became apparent from these preliminary trials that the suspensions of tetraiodophthalimidoethanol were easier to take than barium sulfate suspensions. The patients found the taste of the suspension of the iodinated medium comparable to that of milk of magnesia.

The increased palatability of suspensions of tetraiodophthalimidoethanol over barium sulfate suspensions was brought out particularly well in a student experiment that was conducted on the relative rates of passage of white and "peeled wheat" breads through the stomach. In the course of this work, measured amounts of the two kinds of bread were soaked in the suspension of either barium sulfate or of tetraiodophthalimidoethanol and ingested on an empty stomach. After a number of experiments of this type, the student group was unanimously in favor of the use of the iodinated medium. None of the students noted any effects that might be attributed to the series of weekly doses of 20 to 25 grams of tetraiodophthalimidoethanol.

Eighteen hospital cases were examined with the suspension of the iodinated organic medium. Several of these were studied, also, with the aid of barium sulfate meals. In only one instance did the examination with tetraiodophthalimidoethanol disclose a lesion that was not revealed by barium sulfate. In this case there was an area in the small intestine that was delineated by tetraiodophthalimidoethanol but not by barium sulfate; there was no opportunity to confirm this observation.

Several of the patients examined with tetraiodophthalimidoethanol were in terminal stages of disease, and in two cases it was possible to study autopsy material. In these patients there was no evidence of the medium in the intestine, nor were there any findings that could be attributed to the use of the medium.

At no time did any of the patients or student investigators find that tetraiodophthalimidoethanol was productive of undue constipation. The consistency of the feces was firmer, as would be expected as a result of adding an undigested solid organic compound, but laxatives were not required for adequate elimination. This comparison with barium sulfate is inadequate, because the retention of normal mobility is due in part to the fact that the greater opacity of the iodinated compound permitted the use of small amounts.

DISCUSSION

The first consideration for any preparation proposed for use as a contrast medium is a proper appraisal of its toxicity. Tox-

growth less than barium sulfate. We think the explanation is entirely a physical one, since the barium sulfate particles were slightly smaller.

We have made some intravenous injections in experimental animals. This is a very interesting experiment because the particle size determines where the particular medium will go, and in EKG measure-

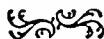
ments there is a convenient tool for determining whether the capillaries of the lungs become plugged. We are going to do some additional work of this sort. We now have a stock of a variety of particle sizes, and we should be able to do a rather polished job on the distribution in the organs of experimental animals.

SUMARIO

El Tetrayodoftalimidoetanol como Medio Gastrointestinal

Estudios comparados de las suspensiones de sulfato de bario y de tetrayodoftalimidoetanol realizados en los perros revelan que el medio yodado facilita una delineación más completa y exacta de las lesiones producidas experimentalmente en el estómago. Los estudios con enemas de doble contraste fueron igualmente más satisfactorios con el medio orgánico yodado

que con el sulfato de bario. Una limitada prueba clínica con el tetrayodoftalimidoetanol demuestra que el nuevo medio posee sabor más agradable que el sulfato de bario, y es aparentemente igualmente inocuo. El empleo ulterior del tetrayodoftalimidoetanol depende del resultado de las comparaciones analíticas con el sulfato de bario en casos clínicos.



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260 Crittenden Blvd
Rochester 7 N Y

DISCUSSION

Ray Carter, M.D. (Los Angeles, Calif) One can only discuss this paper optimistically, and perhaps wishfully, because of the well known deficiencies of our ordinary barium medium. Attempts to improve the qualities of barium have met with only moderate success, and now, when mucosal pattern studies are crucial, any potential improvement is of great interest. As a matter of fact, improvement doesn't have to be outstanding, as this appears to be at first sight. Even if it gives a reasonable improvement of our roentgenologic images, it will be well worth while.

The cost of course, always has to be considered, but there are fallacies there. The cost of the opaque material is a minor part of the cost of an examination. Any reasonable added expense would actually be an economy if it increased the information obtained.

Thorium dioxide sol has served well in the alkaline medium of the colon, but we do not yet have a contrast substance that shows so clearly the mucosal pattern in the stomach. It will be interesting to see what mucosal pattern will be revealed in the small intestine by this new medium. Here again minute details are crucial.

Again one can only hope this medium will prove to be safe, reasonable, economical, and thoroughly useful.

Robert R. Newell, M.D. (San Francisco, Calif) Of course, I have no experience with this material. I have been discouraged about the shortcomings of barium, and many years ago I made some experiments with alginate acid to keep barium from settling out. They were very successful but I never had the energy to complete them. Maybe I will some day.

Various things ought to be investigated of course if barium seems sufficiently unsatisfactory that one could really afford to spend ten dollars a patient in order to get some other material which might be slightly better.

We have tried umbrathor, the less expensive thorium dioxide suspension, for contrast enemas we were told that it had the advantage that it precipitated out on the mucosa. It does but that is a disadvantage rather than an advantage, so we have

returned to barium for contrast studies. I was interested to see the very high smears obtained around the inside of the colon in dogs. If this material proves to smear itself over the inside of the large intestine better than barium does, I should say that it would be very well worth using for contrast enemas, because I think that the search for polyps in the colon now leaves us with too many oversights. We could afford to spend almost any amount of time and effort to better our percentage of success in that region.

Maurice Feldman, M.D. (Baltimore, Md) I would like to ask Dr Strain what effect this medium has on other structures of the body, whether he has made any blood studies, and whether there is any iodine absorption, and how the drug is eliminated.

Hans Armin Jarre, M.D. (Detroit, Mich) There is no need of repeating again the disadvantages which we have encountered with barium, but it is a pleasure to hear that some efforts are being made to obtain a better contrast medium. In that respect it might be worth while to reopen a chapter which has been given very little attention during the past.

There is one chemical at least available which is excreted by the gastric mucosa neutral red. Some years ago I persuaded the University of Wisconsin and Dr Pohle to experiment with neutral red, combining iodine in various forms with derivatives of this chemical and while the results were not successful in the sense that they were practical in radiologic application, it was nevertheless possible to obtain a faint accumulation of such chemicals in the gastric mucosa and probably in the gastric glands themselves.

It is quite possible that research, as we have heard today, may be conducted along similar lines and that the possibilities of excretion of contrast material by the gastric wall may be re-investigated so that functioning areas may be more readily differentiated from non-functioning areas—that normal areas may be differentiated from pathological areas.

William H. Strain, Ph.D. (closing) We don't know all the answers on the pharmacology of tetraiodophthalimidoethanol but we do know that it is not absorbed to any extent. We have had a number of blood iodine determinations made and expect to have some further analyses carried out, to date all have been in the physiological range. The particle size will influence somewhat the amount of absorption, and until we have decided on just the particle size we shall want to use there is no particular point in further studies.

As brought out in the paper we have incorporated the medium in diets of rats—a sort of standard procedure with many new drug preparations—to see how it influenced the rate of growth. To our surprise tetraiodophthalimidoethanol retarded the

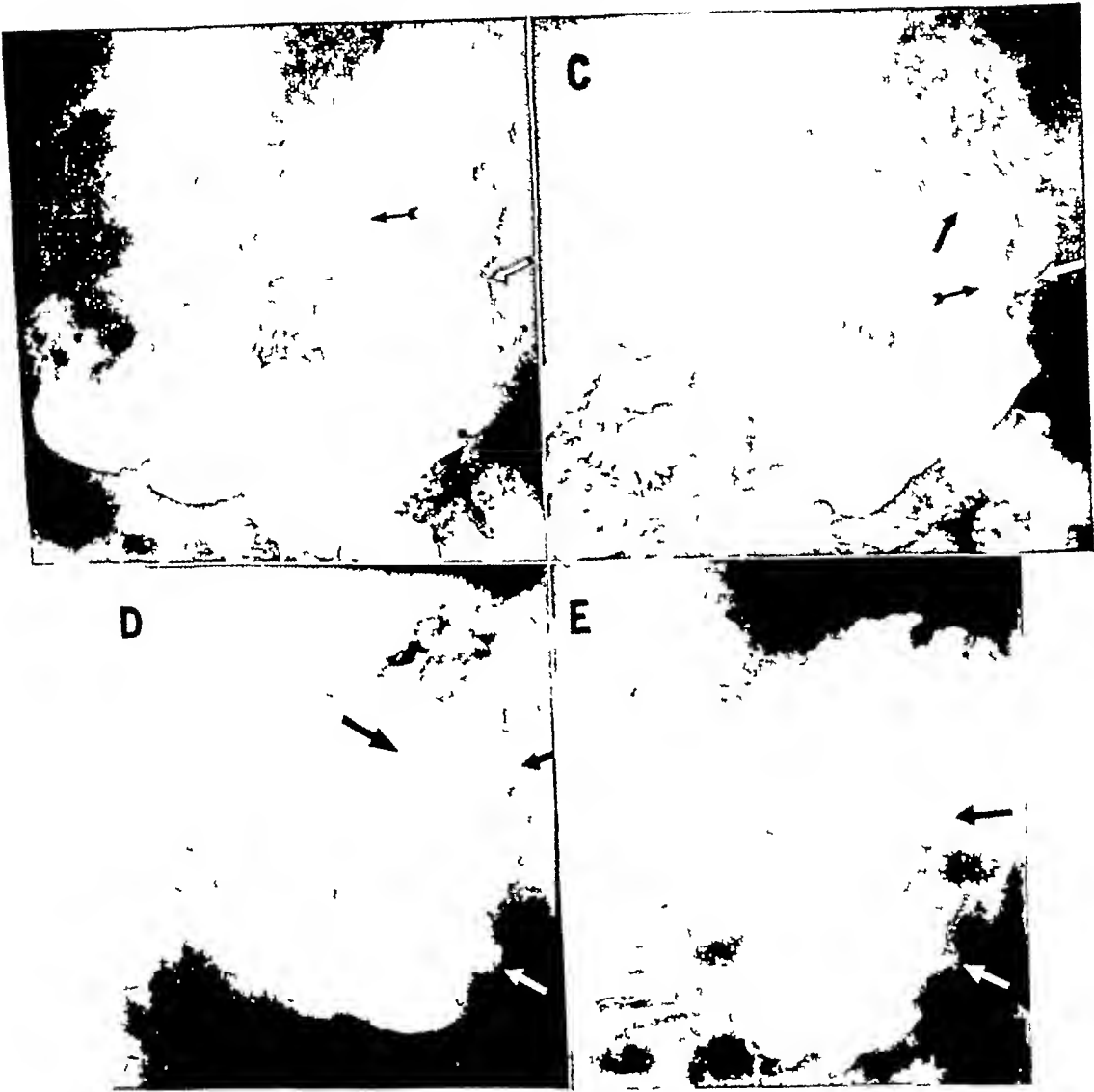


Fig 1 B-E Case 1 Later views Two months after Fig 1 A the deformity persisted but there was no progression (B C) Six months later (D E) there was marked enlargement of the folds with a pseudo neoplastic type of filling defect of the greater curvature (arrows)

likewise revealed evidence of markedly enlarged mucosal folds but no ulceration or neoplasm was seen Two months later another roentgen study of the stomach was made showing persistence of the unusually marked hypertrophic enlargement of the mucosal folds There were a pseudo ulcer filling defect and a large excavated area on the greater curvature of the cardia and fundus The pylorus was spastic and the duodenal cap presented an irregular filling defect with thickened mucosa The colon was also spastic Six months after the original x ray study, re examination of the stomach revealed a large neoplastic like infiltration invading and reducing the lumen of the stomach

Comment In spite of the increasing

enlargement of the filling defect and encroachment upon the lumen of the stomach, the patient has progressively gained in weight and strength and has been asymptomatic for over eighteen months She refused surgical exploration The x-ray findings were out of all proportion to the clinical manifestations, and a diagnosis of hypertrophic giant mucosal folds was made Although the diagnosis is still not absolute, the patient's condition in all probability is of a benign nature Because of the roentgen evidence of extensive

Mucosal Deformities of the Greater Curvature of the Stomach¹

MAURICE FELDMAN, M D

Baltimore, Md

IRREGULARITIES of the greater curvature are commonly observed in the routine roentgen examination of the stomach. Normally the silhouette of the greater curvature is smooth in contour, but occasionally it will present a slightly corrugated, serrated, or cog-wheel appearance due to prominence of the mucosal folds. These serrations are usually regular and rounded in contour. In pathologic conditions of the gastric mucosa the serrations along the greater curvature become enlarged, widened, and irregular. In cases of peptic ulceration associated with gastritis the folds often become very prominent. When the gastric mucosa is greatly hypertrophied, the folds on the greater curvature appear thickened, irregular, and spiked, while the spaces between the folds are markedly widened. These enlarged gastric mucosal folds are best seen on the greater curvature, the lesser curvature usually retains its smooth contour. This is due to the horizontal arrangement of the folds on the lesser curvature, whereas the folds on the greater curvature run at right angles and are transverse or oblique.

Since the study of the gastric mucosal folds has become a routine part of the examination of the stomach, the various changes occurring in the normal and pathologic states must be properly interpreted and differentiated. Numerous diagnostic problems have been encountered following the demonstration of deformities of the greater curvature, resulting from the changes in the mucosal folds. The normal mucosal folds may be redundant and hang down from the cardia of the stomach, producing a filling defect. At times the gastric folds become tremendously enlarged and produce a filling defect on the greater curvature simulating a neoplasm.



Fig 1 A Case 1 Marked deformity of the greater curvature with enlargement of the mucosal folds. See Fig 1 B-E

In this paper nine cases are reported, presenting digestive symptoms and abnormal roentgen findings of the greater curvature of the stomach which conformed to no distinct disease pattern.

CASE REPORT

CASE I A woman aged 56 gave a six months history of weakness, weight loss of 30 pounds, vertigo, anorexia, nausea, and constipation. On physical examination she appeared undernourished, with evidence of a considerable loss of weight. The abdominal examination was negative and no mass was felt. Laboratory findings revealed a secondary anemia, normal urine and negative Wassermann reaction. Gastric analysis showed a total acidity of 40 and free hydrochloric acid 20.

A gastro intestinal roentgen study disclosed a large, irregular, ulcerating filling defect on the greater curvature of the stomach simulating a malignant neoplasm and unusually large hypertrophied mucosal folds. Gastroscopic examination

¹ Presented at the Thirty second Annual Meeting of the Radiological Society of North America Chicago Ill., Dec 1-6, 1946

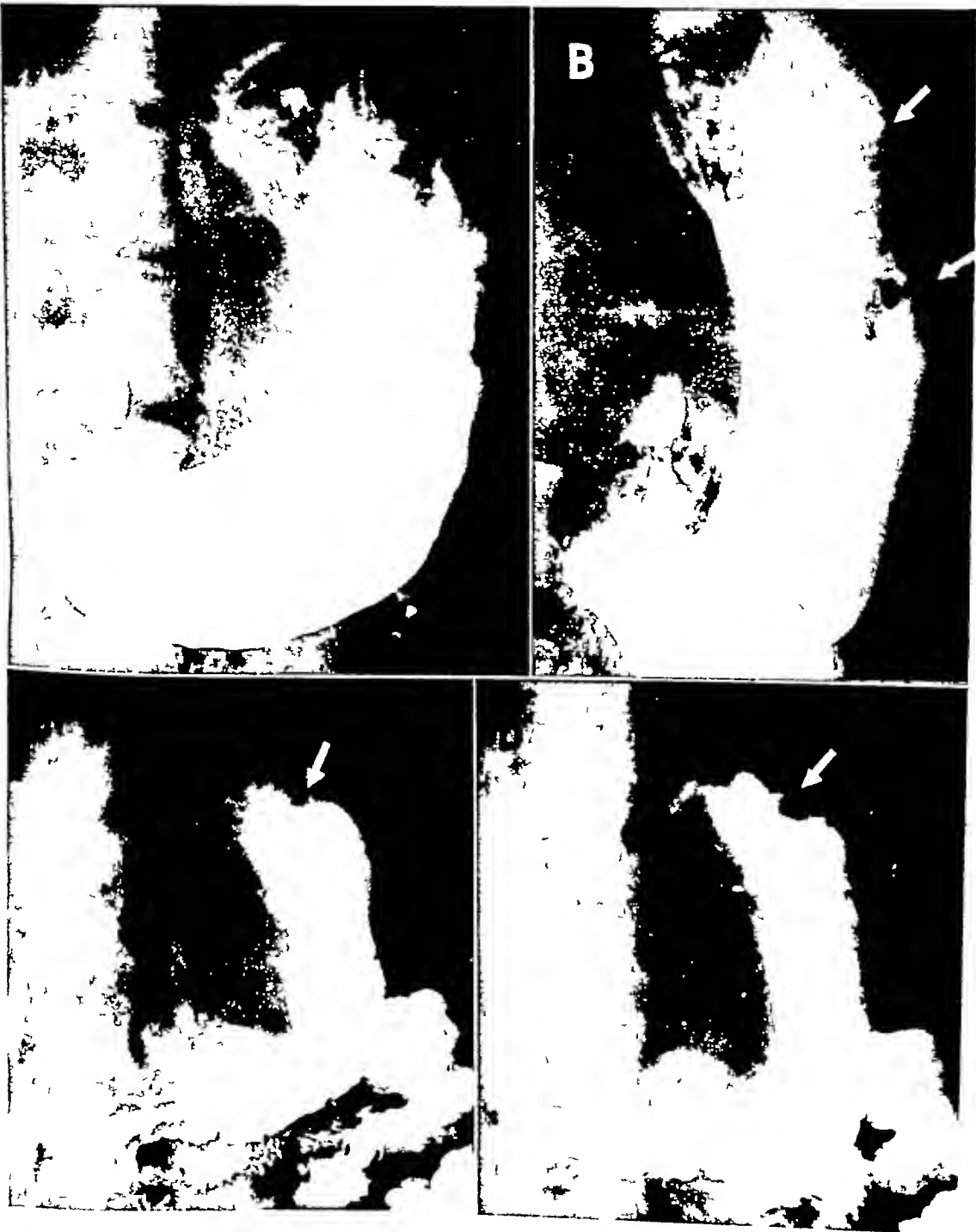


Fig 3 A B Case 3 A An extensive irregular filling defect is shown on the greater curvature of the cardia and fundus of the stomach B Lateral view presenting greater detail of the mucosal enlargement and deformity (arrows)
C D Case 4 Deformity of the greater curvature of the cardia and body of the stomach due to the enlarged mucosal folds

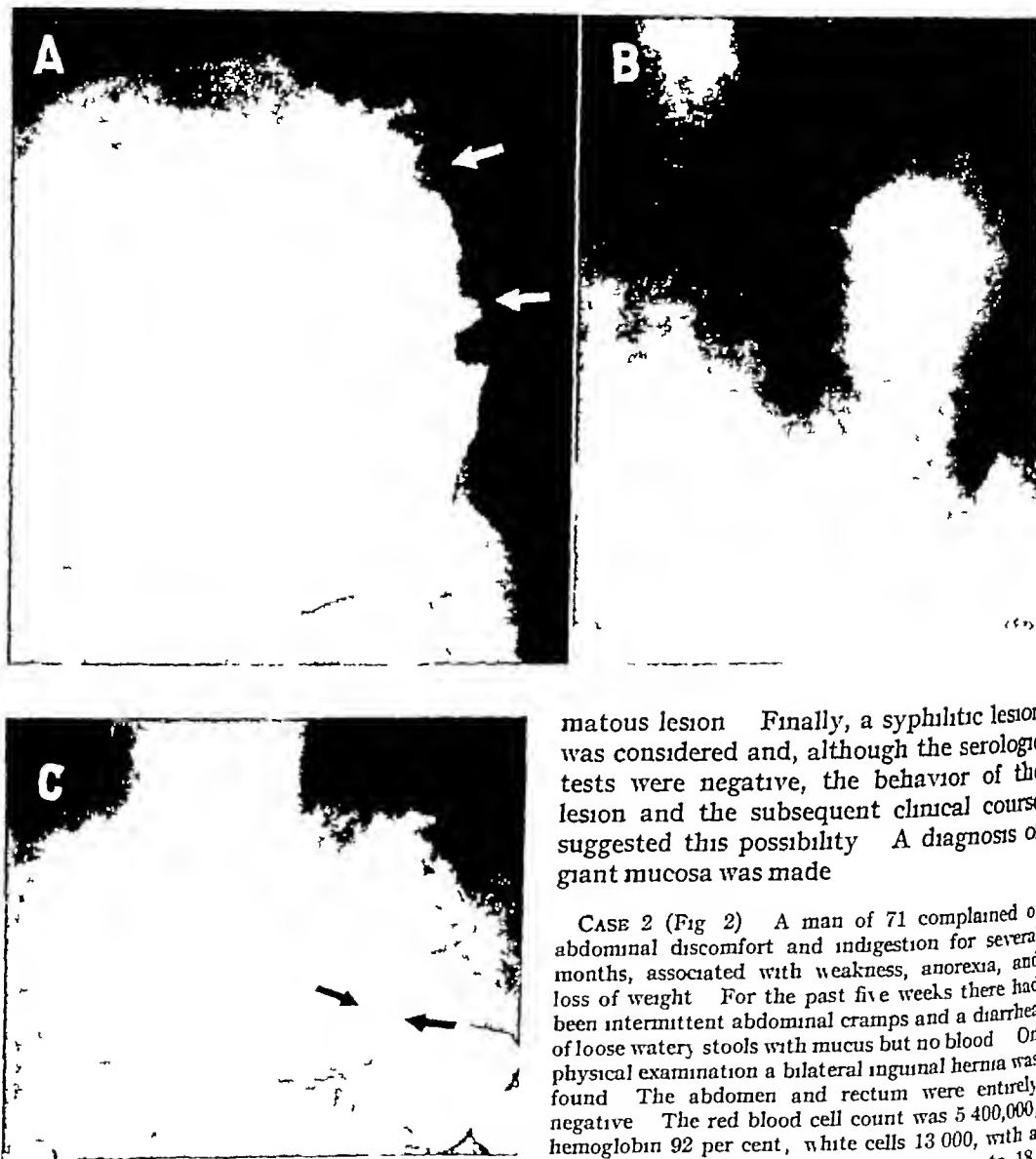


Fig 2 Case 2 A Extensive deformity on the posterior wall of the greater curvature B Roentgenogram made six months later in the erect position showing the extensive filling defect with mucosal changes C Partially filled stomach illustrating the pseudo ulcer niche-defect at arrows

mucosal involvement and hypertrophy, carcinoma was eliminated and the presence of a lymphoblastomatous lesion was strongly considered. Roentgen studies showed a progressive invasive type of filling defect, but no mass could be palpated corresponding to the defect. This finding, too, is consistent with a lympho-

matous lesion. Finally, a syphilitic lesion was considered and, although the serologic tests were negative, the behavior of the lesion and the subsequent clinical course suggested this possibility. A diagnosis of giant mucosa was made.

CASE 2 (Fig 2) A man of 71 complained of abdominal discomfort and indigestion for several months, associated with weakness, anorexia, and loss of weight. For the past five weeks there had been intermittent abdominal cramps and a diarrhea of loose watery stools with mucus but no blood. On physical examination a bilateral inguinal hernia was found. The abdomen and rectum were entirely negative. The red blood cell count was 5,400,000, hemoglobin 92 per cent, white cells 13,000, with a normal differential count, sedimentation rate 18. Stools were negative for blood, and cultures were negative for pathogens. The Wassermann reaction was negative.

A gastro-intestinal roentgen study revealed enlarged mucosal folds with a suggestive ulcerative defect on the greater curvature of the stomach. The duodenal cap appeared regular. A colon enema study revealed no organic lesion. Six months later a check up examination showed an apparent extensive infiltrative lesion of the fundus and cardia of the stomach with widening of the mucosal folds. One month after this re-examination by another roentgenologist was also reported as demonstrating enlargement of the gastric mucosal folds. The gastroscopic examination revealed evidence of a gastritis

intermittent abdominal cramps with gurgling due to excessive gas, vomiting, and loss of weight. There was a marked progressive constipation, relieved by laxatives and enemas. Physical examination showed a palpable mass in the left upper abdomen. Blood examination showed red cells 4,000,000, hemoglobin 88 per cent, white cells 7,500, differential count normal, sedimentation rate 42. Urine and serologic examinations were negative. Gastric analysis revealed an absence of free hydrochloric acid. Stools showed a trace of blood.

The gastro intestinal roentgen study demonstrated an extensive deformity of the greater curvature with hypertrophy of the mucosal folds of the cardia and fundus of the stomach. A trace of barium was retained in the stomach at the end of five hours. Twenty-four hour examination showed a filling defect at the splenic flexure. A barium enema revealed an annular filling defect at the splenic flexure with partial obstruction due to carcinoma. At operation a carcinoma of the colon was resected. The stomach was not opened but was explored and revealed no evidence of gastric disease.

CASE 6 (Fig 5) A man aged 56 complained of loss of weight and weakness for over one year. During this period a chest film revealed a large mass in the mediastinum and in the right lower lung. There was involvement of the cervical lymph nodes and biopsy revealed metastatic carcinoma. Three weeks prior to a gastro intestinal roentgen study the patient began to have pain in the abdomen, radiating to the back and associated with severe constipation.

The x-ray revealed an extensive deformity of the greater curvature with unusually broad flattened folds in the fundus of the stomach. The gastric mucosal folds were thinned out and reduced in number. The upper jejunum showed a flattening of the folds, indicating evidence of a nutritional deficiency. A twenty-four-hour examination showed a poorly filled colon. A barium enema revealed an extensive carcinoma of the splenic flexure. At operation the tumor was resected. The stomach was not incised, but exploration revealed no evidence of a gastric lesion.

Comment Cases 5 and 6 presented roentgen changes in the mucosal folds of the stomach. The folds were widened and hypertrophied. In each, extensive deformity of the greater curvature simulated carcinoma, the colon revealed a carcinoma of the splenic flexure, and the growth was resected. The stomachs were explored but not opened, as nothing was found to warrant incising them. The patient with metastasis to the mediastinum and lung died, the other is living and well ten months after the operation.



Fig 5 Case 6. An extensive deformity of the greater curvature with marked widening of the mucosal folds.

CASE 7 (Fig 6, A and B) A woman aged 61 complained for several months of substernal pressure and distress following meals. She felt better when her stomach was empty. There was no vomiting. There were considerable gas and constipation. The physical examination was negative.

A gastro intestinal roentgen study revealed a small penetrating ulcer defect on the greater curvature. There was an extensive deformity of the greater curvature with marked enlargement of the mucosal folds as a result of a gastritis. The lesser curvature was regular, the pylorus was spastic and the duodenal cap was normal. The colon showed evidence of stasis. A diagnosis of a penetrating ulcer of the greater curvature of the stomach associated with gastritis was made.

Comment In this case there was an extensive deformity of the greater curvature of the stomach with an ulcer-niche-like filling defect. The picture varied with the state of filling of the stomach. When it was completely filled, there was a concave deformity with an ulcer-niche-like defect projecting out from its center. With partial filling, the entire greater curvature was ragged and irregular. No gastroscopic examination was obtained. The clinical picture was indeterminate,



Fig. 4 Case 5 A Ulcerating type of filling defect on the greater curvature (arrows), also some deformity of the greater curvature of the cardia B Same case with small amount of barium showing a more extensive deformity (arrows)

The patient was placed on medical therapy and has been followed for fifteen months. He has regained his weight, symptoms have disappeared, and there have been no further digestive upsets.

Comment This case presented a clinical picture of carcinoma, with a short history of digestive disturbance and loss of weight and strength. The x-ray revealed enlarged, widened, and flattened mucosal folds, the greater curvature of the stomach was irregularly deformed and presented a pseudo-ulcer filling defect, which apparently was produced by the enlarged irregular mucosal folds. Cancer was suspected on the basis of the clinical history and roentgen findings but, owing to the presence of enlarged mucosal gastric folds, this diagnosis seemed to be questionable, and further studies were recommended. Since the gastroscopic examination revealed the mucosal changes but no evidence of neoplasm, the roentgen findings were believed to be of a benign character. The subsequent clinical course also suggested the probability of a benign condition.

CASE 3 (Fig 3, A and B): A man aged 47 complained of pain in the right upper quadrant for ten years. The pain did not radiate and there was no relationship to food. His appetite was good and bowels regular. There was no vomiting. The left kidney had been removed ten years earlier for kidney stones.

A gastro intestinal roentgen examination showed a deformity on the posterior wall of the greater curvature of the cardia associated with giant mucosal folds. The lesser curvature was regular, the pylorus was spastic, the prepylorus showed a transient narrowing due to spasm. The duodenal cap was normal. A trace of barium was retained in the stomach at the end of five hours. Motility of the intestine was normal, the colon was negative. The extensive filling defect on the greater curvature of the cardia of the stomach was believed to be due to giant mucosal folds.

CASE 4 (Fig 3, C and D): A man aged 65 complained for many years of digestive disturbances with pain across the abdomen, made worse by eating. There was intermittent diarrhea but no vomiting. The physical examination was negative. A gastro-intestinal roentgen study revealed enlargement of the gastric mucosal folds with a persistent deformity of the greater curvature of the cardia of the stomach which strongly suggested an early neoplastic lesion.

Comment Cases 3 and 4 presented dissimilar symptoms, but the roentgen findings were characteristic of an intragastric abnormality involving the greater curvature of the cardia and body of the stomach. In each instance the roentgen features simulated a malignant growth. Each presented enlarged mucosal folds. No gastroscopic examination was made. It has been over eighteen months since the roentgen examination, and both patients are asymptomatic.

CASE 5 (Fig 4): A man aged 60 complained for one year of pain in the epigastrium and back,

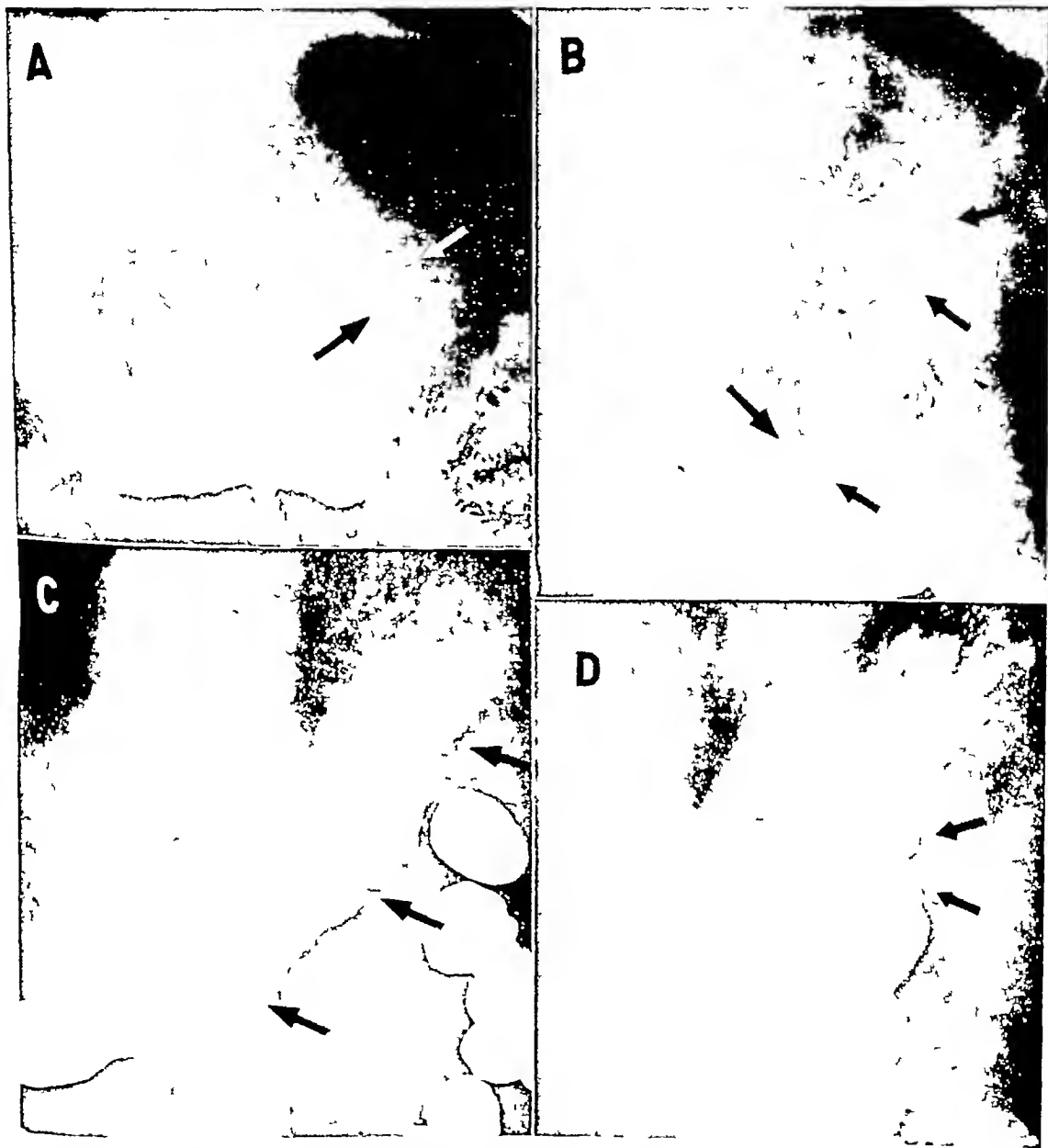


Fig 7 A B Case 8 A Marked deformity of the greater curvature with a pressure defect due to distention of the splenic colon B Roentgenogram made in erect position showing the extent of the deformity on the greater curvature with a deep penetrating ulcer niche on the lesser curvature of the antrum (arrows)
C D Case 9 C Case of duodenal ulceration Exaggerated serrations or saw tooth effect of the greater curvature D Oblique view showing the deformity of the greater curvature with pseudo ulcer niche defects (arrows)

caution must be taken in the interpretation of mucosal abnormalities and filling defects of the greater curvature of the stomach. This is especially important in the cases presenting defects that do not conform to the usual disease pattern. Repeated roentgen studies are essential in all

doubtful cases and confirmatory information obtained by thorough clinical investigation and gastroscopic studies is necessary. An unequivocal diagnosis cannot always be made solely on the basis of the gastric roentgen findings. A study of the subsequent clinical developments over a

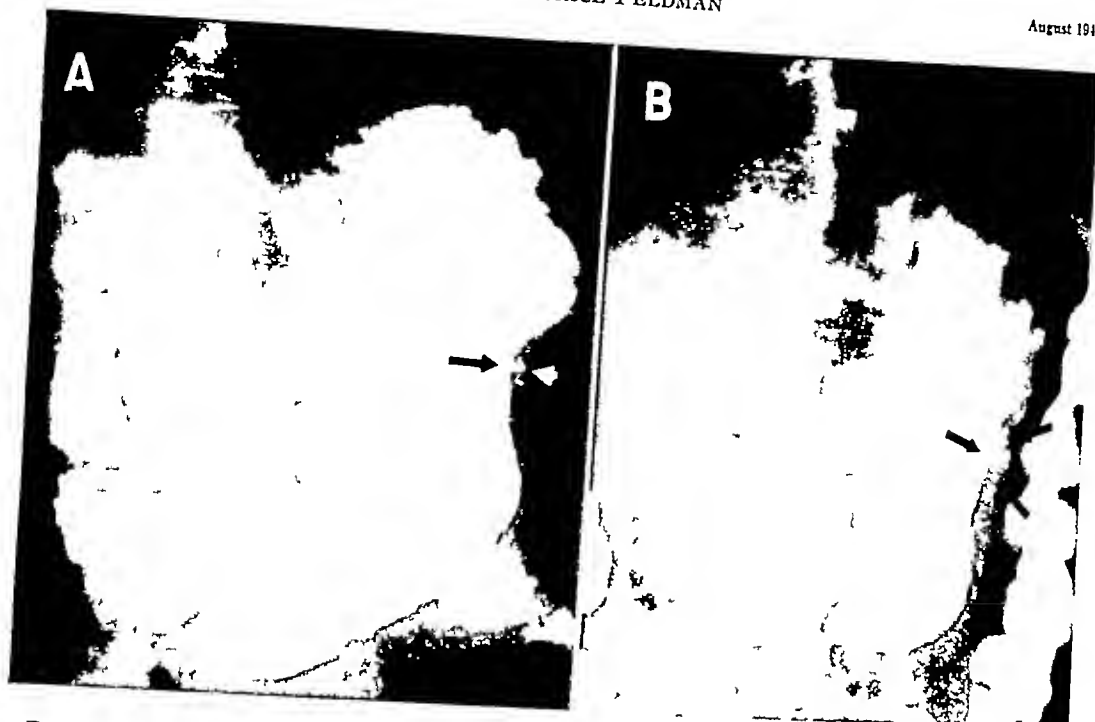


Fig 6 Case 7 A An ulcer-like niche defect in an excavated area on the greater curvature (arrows)
B Same case with partial filling of the stomach, showing marked deformity due to enlarged mucosal folds.

and since there was no loss of weight and nothing to indicate a serious gastric disease, the patient was placed under medical therapy and observation. On clinical follow-up examination, eight months later, she was asymptomatic.

CASE 8 (Fig 7, A and B) A man aged 66 complained of vague stomach disturbances for eleven years, giving a history of periodic episodes of epigastric pain occurring about two hours after meals, nausea, belching and constipation. His appetite was poor; there was no loss of weight. Two years after the onset of symptoms, x-ray studies revealed a normally functioning gallbladder without stones.

A gastro intestinal roentgen examination showed marked intestinal stasis but no gastric lesion. The patient's symptoms were relieved and he felt comparatively well until six months later when digestive disturbances recurred. A gastro intestinal roentgen examination made at this time revealed an extensive deformity of the greater curvature of the cardia and the fundus of the stomach with evidence of enlargement of the mucosal folds. A deep penetrating ulcer niche defect was noted on the lesser curvature of the antrum of the stomach. A diagnosis of a penetrating gastric ulcer associated with gastritis was made.

CASE 9 (Fig 7, C and D) A man aged 47 gave a history of indigestion for fifteen years with

intermittent pain relieved by food. Physical examination was negative. A gastro-intestinal roentgen study revealed normal emptying of the stomach. The greater curvature was ragged, with deep irregular serrations. A mucosal study showed some hypertrophy of the folds. The lesser curvature was regular. In the erect oblique position a large excavating filling defect with two small niche like projections was demonstrable. The pylorus was spastic and the duodenal cap markedly deformed due to an ulceration. A diagnosis of duodenal ulceration with associated hypertrophic gastritis was made.

Comment These two cases, one a gastric ulcer and the other a duodenal ulcer, presented gastric mucosal changes indicating an associated gastritis. Each presented a bizarre appearance of the greater curvature, suggesting an organic gastric disease. Each was due to an associated gastritis. No gastroscopic examination was made. Both patients were asymptomatic one year after the roentgen examination.

SUMMARY

The purpose of this paper is to point out and emphasize the fact that the greatest

están casi siempre obliterados Sin embargo, dichas alteraciones podrían encajar en el cuadro de la enfermedad de Hodgkin (linfoblastomatosis) o de la sífilis Una gran hiperplasia de los pliegues de la mu-

cosa es compatible con un estado benigno Una malformación extensa de la curvatura mayor con bordes serrados muy bien definidos puede deberse a gastritis asociada a úlcera péptica



period of months is essential and often necessary to establish the significance of non-conforming disease patterns presenting deformities of the greater curvature

A group of unusually interesting cases is presented to illustrate some of the difficulties encountered in the roentgen diagnosis of non-conforming disease patterns of the mucosa of the stomach. The filling defects shown in the roentgenograms were strongly suggestive of a primary gastric lesion. The presence of marked hypertrophy of the gastric mucosal folds is not ordinarily consistent with carcinoma. In carcinoma the folds are usually obliterated. However, these changes could fit into the picture of Hodgkin's or lymphoblastomatous disease and syphilis. Great enlargement of the mucosal folds due to hypertrophy is consistent with benign giant gastric mucosa. Extensive gastric deformity of the greater curvature with unusually marked serrations may be due to a gastritis associated with peptic ulceration.

2425 Eutaw Place
Baltimore 17 Md

DISCUSSION

Kenneth S Davis, M D (Los Angeles, Calif)
Dr Feldman is to be congratulated for bringing out a problem in differential diagnosis that all of us have

encountered. I feel that his paper is timely and thought-provoking. Like Dr Feldman, we at St Vincent's Hospital have felt that a gastroscopic study is essential in those cases with borderline and atypical roentgen findings. We also agree with him in insisting on repeat x-ray studies where the roentgen evidence of a lesion is not definite and clearcut.

At times there are lesions of the stomach which cannot be definitely diagnosed even by combined x-ray and gastroscopic studies. We have found that in these cases a peritoneoscopic study, as developed by Dr Ruddock, is of great help in the differentiation between benign and malignant lesions, as well as in ruling out metastasis.

In this study, which is done on an empty stomach, the patient swallows a duodenal tube with a light bulb at the tip. Peritoneoscopy is then done with the stomach empty. Air is then slowly pumped into the stomach while it is observed under the peritoneoscope. If the lesion in the stomach wall is indurating, this part of the stomach does not expand and the lesion can be localized. When the stomach is partially filled with air, peristalsis can be observed and its presence or absence may be determined in any portion of the organ. When the stomach is well distended with air, the light within the stomach is turned on and the light in the peritoneoscope turned off. This procedure gives a minute and detailed view of the stomach wall. The gastric rugae when normal are never visualized, but when hypertrophied they can be plainly seen. The blood vessel markings are closely observed as they are the clue to lesions of the stomach wall. In the presence of an indurating lesion the circulation is definitely interrupted. I believe this procedure is preferable to exploratory surgery as it entails practically no operative mortality.

SUMARIO

Malformaciones de la Mucosa de la Curvatura Mayor del Estómago

Tiene por fin este trabajo señalar y recalcar la suma cautela que hay que mostrar en la interpretación de las anomalías y nichos de la mucosa de la curvatura mayor del estómago, máxime en los casos en que no se conforman al habitual patrón patológico. En todo caso dudoso se imponen repetidos estudios roentgenológicos y se necesitan datos corroboradores aportados por la investigación clínica detenida y los estudios gastroscópicos. No puede formularse siempre un diagnóstico firme a base exclusiva de los hallazgos radiológicos del estómago. A fin de establecer el significado de los patrones patológicos

atípicos en las malformaciones de la curvatura mayor el estudio de los fenómenos clínicos subsiguientes durante varios meses resulta indispensable.

Preséntase un grupo de casos por demás interesantes para demostrar algunas de las dificultades con que tropieza el diagnóstico roentgenológico de los cuadros patológicos atípicos de la mucosa gástrica. Los nichos que aparecen en los roentgenogramas son muy indicativos de lesión gástrica primaria. La presencia de hipertrofia pronunciada de los pliegues de la mucosa gástrica no suele ser compatible con carcinoma, pues en éste los pliegues

están casi siempre obliterados Sin embargo, dichas alteraciones podrían encajar en el cuadro de la enfermedad de Hodgkin (linfoblastomatosis) o de la sífilis Una gran hiperplasia de los pliegues de la mu-

cosa es compatible con un estado benigno Una malformación extensa de la curvatura mayor con bordes serrados muy bien definidos puede deberse a gastritis asociada a úlcera péptica



Carcinoma of the Tonsil

A Review of Treatment and Its Results in a Group of Ninety Cases

JOHN H. WALKER, M.D., and MILFORD D. SCHULZ, M.D.¹

THE TONSILLAR area is a relatively uncommon site for cancer. Because of this fact, the medical literature contains few reports covering a large number of cases. From the material which has been published (3, 5, 9, 10, 11), it is apparent that the pattern of management of patients with this disease has been fairly uniform for the past fifteen years. Since progress depends on a periodic evaluation of the results of any treatment, it has seemed worth while to review at this time a group of cases with the diagnosis of carcinoma of the tonsil treated with irradiation during the past ten years.

MATERIAL STUDIED

This study is based on all the patients with carcinoma of the tonsil irradiated at the Collis P. Huntington Memorial Hospital from 1936 through 1941 and at the Massachusetts General Hospital from 1936 through 1945. Since the primary site of an extensive tumor in the mesopharynx is often impossible to determine, only those cases in which it was reasonably certain that the lesion was located at the palatine tonsil, the tonsillar fossa, the tonsillar pillars, or in the triangular fold have been considered. Excluding one case in which the tumor later proved to be a Kaposi sarcoma, 90 cases were found and analyzed.

In the series, there were 76 (84 per cent) males and 14 (16 per cent) females. The median age was sixty-five, the oldest patient being eighty-seven and the youngest twenty-nine years. These figures correspond with those reported by Schall (9) and Lierle (5), and confirm the common belief that cancer of the tonsil occurs most frequently in males in the seventh decade of life.

Because of the insidious onset of malignant disease, patients almost universally procrastinate in seeking medical advice. The median delay in treatment in this group was three months. The duration of disease (symptomatically) at the time treatment was instituted ranged from one day (?) to over two years. The most frequent presenting complaint was soreness of the throat, which was noted in 54 per cent of the group. Swelling of the neck was the first sign in 46 per cent, difficulty in swallowing in 16 per cent, bleeding in 15 per cent, weight loss in 4 per cent, and hoarseness in 2 per cent. A noteworthy fact is that in only 9 per cent was a growth in the mouth observed.

Lymph-node metastases are often the first indication to the patient that he has the disease. Sixty per cent of the group presented enlarged nodes when they were first seen, and in two-thirds of these the "lump in the neck" was the first subjective sign to be observed. Of those who had no palpable metastases at the time of first examination, 8 per cent later showed cervical lymph node involvement. No attempt has been made to correlate the metastatic spread of the cancer with the grade of malignancy of the lesion, but the evidence suggests that tumors classified as Grade I (Broders) did not metastasize early, although they were locally recalcitrant in responding to irradiation. One patient with transitional-cell carcinoma had generalized metastases when first seen, and in another metastases subsequently developed beyond the cervical nodes. Of the patients with lympho-epithelioma, one had remote disease and three had cervical metastases when first seen.

¹ From the Department of Radiology, Massachusetts General Hospital, Boston, Mass. Accepted for publication in December 1946. Presented at the First Annual Meeting of the Pacific Northwest Radiological Society, May 4, 1947.

HISTOLOGY OF TUMORS

(Table I)

Of the total group, 78 tumors were epidermoid carcinomas of varying grades, 7 were lympho-epitheliomas, 3 transitional-cell carcinomas, 1 a lymphosarcoma, and 1 a reticulum-cell sarcoma. Carcinoma of the tonsil is, as a rule, of a high degree of malignancy, only a small percentage being of the highly differentiated type. In the present series, the 8 per cent of low-grade malignancy corresponds to the incidence reported by Duffy (3) and by Martin and Sugarbaker (6). Taylor and Nathanson (11), on the other hand, reported 17 per cent Grade I lesions.

TABLE I TUMORS OF THE TONSIL ANALYSIS HISTOLOGIC

Epidermoid carcinoma	
Grade I	8%
Grade II	28%
Grade III	30%
Grade IV	3%
Unclassified	18%
Lympho-epithelioma	8%
Transitional cell carcinoma	3%
Sarcoma	2%

TREATMENT

The methods of treatment carried out at the Huntington Memorial Hospital and at the Massachusetts General Hospital have, on the whole, been comparable. Neck dissection was employed in none of the 90 patients in the present series. Already existing metastases, or the fact that the patients were poor surgical risks, precluded attempted cure by dissection.

Adherence to inflexible rules or to definite specifications in radiation therapy is inadvisable. Individual evaluation as to the course and method of irradiation has been the policy in use at both clinics. In general, as much radiation is directed into the tumor as can be safely tolerated by the overlying tissue. In many instances, since palliation only was sought, cancericidal doses were avoided.

During the ten-year period under consideration, both supervoltage and high-voltage therapy were employed. A number of patients received both. Occasional

cases in which high-voltage therapy apparently failed were subsequently treated with supervoltage. Especially was this true of patients in whom cervical metastases subsequently developed or cervical metastases already present failed to respond well to the lower voltage. The change to higher voltage was made, for the most part, in an effort to produce as little further damage as possible to previously irradiated skin.

With high-voltage (200 kv) treatment, the factors used were 50 cm tube-skin distance, 20 ma, with 0.5 mm Cu and 1.0 mm Al filter, half-value layer 0.9 mm Cu, roentgen output 50 per minute, and portals adequate to cover the disease, sparing as much normal tissue as possible. Ordinarily two opposing portals were employed, supplemented in some cases by an intra-oral cone at 30 cm distance.² The optimum dose appeared to be 3,000 to 4,000 r, measured in air, through each side, at the rate of 300 r per day. When an intra-oral cone was used, an additional 2,500 to 3,000 r were delivered at 300 r per day.

With supervoltage (1,000 kv at Huntington Hospital, 1,200 kv at Massachusetts General Hospital), the tube-skin distance was 70 cm and the half-value layer was 9.0 mm Cu. Treatments were given daily at the rate of 300 to 400 r per treatment through a single lateral portal. A total dose varied from 2,400 to 6,600 r, the optimum dose being considered to be 6,000 r, measured in air, at the skin level.

Twelve patients received interstitial radiation in conjunction with roentgen therapy. In some cases, this additional treatment was administered to the primary lesion, in others to lymph nodes involved by metastases.

A routine procedure followed in this clinic is the extraction of remaining teeth, prior to irradiation, in patients with poor oral hygiene, or even when the remaining

² Treatment with the intra-oral cone was employed in those cases in which it was mechanically possible to introduce it, and in which the primary disease could be covered with the cone.

TABLE II TUMORS OF THE TONSIL SURVIVAL OVERALL

Years Survival	No Patients with Opportunity to Survive	No Patients Who Survived
1	70*	42 (53%)
2	66	26 (39%)
3	56	14 (25%)
4	40	9 (18%)
5	39	6 (15%)
6	25	3 (12%)
7	21	3 (14%)
8	15	2 (13%)

* Eleven patients did not have opportunity to survive 1 year and are not included in this analysis

teeth are healthy This is based on the well accepted fact that teeth undergo definite changes when exposed to x-rays or to gamma radiation (2, 8) The patients, as a rule, are co-operative when adequate explanation is offered them

RESULTS OF TREATMENT

At the end of the year 1945, of the 90 patients included in the study, 48 were known to be dead, 11 were untraced, and 31 were known to be alive In the analysis of results of treatment, the 11 untraced patients are counted as having died of cancer as of the date of the last observation, 8 had evident disease at that time Of the 48 known dead, 37 died of cancer, 6 died of intercurrent disease (5 of these, however, had recognized residual cancer), and in 5 the cause and date of death could not be determined Ten patients are alive with evident disease, and 21 are alive without apparent disease

Of the patients who have had a chance to survive five years or more (*i.e.*, were treated five or more years ago), 6 or 15 per cent have done so (Table II) One of these has since died of pulmonary metastases Of 21 patients who had an opportunity to live seven years or more, only 3 have survived that length of time At the end of the first year after treatment, 47 per cent had succumbed to their disease

Of the 21 patients alive and free of disease at the close of 1945, in 3 the period since treatment is less than one year, in 5, it is one to two years, in 3, two to three years, in 4, three to four years, in 2,

four to five years, and in 4 over five years have elapsed since treatment The longest survival, with freedom from disease, is eight years The longest survival among the 10 patients living with disease is five years³

ANALYSIS OF RESULTS OF TREATMENT

Histology of Tumors Analysis of the results of treatment on the basis of the histology and grade of the lesion indicates that prognosis cannot be made on the grade of the tumor alone The tumors histopathologically classified as lympho-epithelioma, as a whole, responded more favorably to treatment than did the epidermoid carcinomas, the transitional-cell carcinomas, or the lymphosarcomas Of 7 patients with epidermoid carcinoma Grade I, none has lived longer than eighteen months, and control of the local disease has been poor All of the patients with epidermoid carcinoma who survived two years or more had Grade II and Grade III lesions In some cases with fairly small primary lesions the local disease failed to be controlled, while in others with larger tumors of the same histologic grade the primary lesion was controlled without difficulty Sixteen patients who had epidermoid carcinoma are living without disease with an average survival of thirty-nine months, 8, alive but with clinical evidence of disease, have an average survival of nineteen months

In 6 of the 31 living patients, the tumor was lympho-epithelioma This type of tumor has shown a most gratifying response to treatment In contrast to the observations of Martin and Sugarbaker (6) that for a patient with lympho-epithelioma the duration of life from the onset of symptoms was only twelve months, in this series it was found to be over thirty months This was true in those surviving with disease as well as those who have remained free of disease

Of 3 patients with transitional-cell car-

³ This patient has since died, sixty three months after treatment

TABLE III TUMORS OF THE TONSIL ANALYSIS WITH RESPECT TO METASTASES

Years Survived	With Metastases (At Time of Treatment)		Without Metastases		
	No with Opportunity to Survive	No	Survived Per Cent	No with Opportunity to Survive	No Survived Per Cent
1	46	20	43	33	22 66
2	41	13	32	25	13 52
3	34	7	21	22	7 32
4	29	4	14	20	5 25
5	23	2	9	16	4 25

cinoma, one is alive twenty-six months after treatment but with questionable disease in the neck, two are dead of generalized metastases twenty-one and twenty-six months, respectively, after the initial therapy. Both patients with sarcomatous lesions are dead: the one with lymphosarcoma survived twelve months, the other, with reticulum-cell sarcoma, died fourteen months after institution of treatment.

Metastases The presence or absence of metastases, as might be suspected, played an important role in the control of the tumor. Table III shows the comparative survival rates for patients with and without metastases at the beginning of treatment. Of those free of metastases when first seen, 66 per cent survived the first year after treatment, whereas only 43 per cent of those with metastases lived this length of time. Twenty-five per cent of those without metastases, who had an opportunity to do so, survived five years as compared with but 9 per cent of the metastatic group. The primary lesion, as a rule, responded to treatment more readily than the metastatic lymph nodes, with the exception of regional cervical metastases from lympho-epithelioma.

Combined Radium and Roentgen Therapy In the group studied, no striking advantage was evident from the use of radium as an adjunct to roentgen therapy. In one of the 12 cases so treated, interstitial radiation and x-rays were employed to control recurrence three years after surgical removal. This patient has survived more than five years without clinical evidence of disease. The average survival of the other 11 patients in the group is 14.5 months as compared with an average survival of 21.5 months for the entire series,

and 12.5 months for those known to be dead. In other words, the results in patients treated in this clinic by interstitial and external irradiation are no better than those in patients treated by external irradiation alone.

Supplementary External Irradiation The question as to the value of supplementary external irradiation in those patients in whom the primary disease was not controlled by the initial course of treatment, or in those who subsequently had a recurrence, is a difficult one to answer. The small number of cases makes consideration of individual results almost a necessity.

Of 12 patients who lived four years or more, 3 required further treatment two to three years after the initial course. One of the 3 survived an additional three years, at the end of which time he died of remote metastases, 2 are still alive and free of disease five years after the second course of treatment. One of the latter two had an uvulectomy and interstitial irradiation at the site of recurrence followed by external irradiation. In the second patient, the recurrence was controlled solely by intensive intra-oral high-voltage therapy.

Three of the 26 patients who survived two years received secondary courses of external irradiation six, eleven, and twenty-four months after their initial treatment. One has since died of his disease, one is free of disease, and one shows questionable disease in a cervical node.

As a whole, patients with recurrence within the first six to twelve months after irradiation were not benefited by further treatment. When, however, recurrence did not appear until more than one year

TABLE IV TUMORS OF THE TONSIL COMPARISON OF RESULTS OF SUPERVOLTAGE AND HIGH VOLTAGE TREATMENT

Years Survived	Supervoltage Radiation		High Voltage Radiation	
	No with Opportunity to Survive	No Survived Per Cent	No with Opportunity to Survive	No Survived Per Cent
1*	36	21 58	43	21 49
2	30	13 43	36	13 36
3	28	9 32	28	5 18
4	26	6 23	23	3 13
5	21	5 24	18	1 6

* Eleven patients treated during 1945 are excluded from this analysis

after the initial treatment, supplemental treatment appeared to be of definite value

Comparison of Supervoltage and High Voltage Treatment Because of reports from other clinics of the great advantage offered by supervoltage as compared to lower-voltage treatment, especial interest was taken in comparing the results of these two methods of irradiation. Of the entire group, 50 patients were treated with high-voltage and 40 with supervoltage radiation. Table IV shows the survival rates in the two groups. Over the ten-year period, for patients having the opportunity to live five years, the percentage of survival was 24 in the group treated with supervoltage and 6 in those receiving high-voltage therapy. The difference between these figures is significant but, in evaluating them, other factors should be borne in mind. First, the number of cases in each group is not large. Second, a division of the ten-year period into two five-year periods showed that, while in the first five years, the survival rate with supervoltage was more favorable than that with high voltage, in the second period the results were roughly comparable. This shift in values is due primarily to a gradual improvement in the method of treatment with high-voltage radiation. Holmes and Schulz (4) report a five-year survival rate with supervoltage therapy of 21 per cent and conclude that this form of irradiation warrants further trial in carcinoma of the tonsil.

DISCUSSION

In the relatively few large series of carcinoma of the tonsil published in recent

years (1, 3, 5, 6, 7, 9, 10), the five year survival rates, ranging from 10 to 17 per cent, are comparable with the 15 per cent rate in the present group. It is significant, however, that in this series almost equally satisfactory results have been obtained without supplementary surgical procedures, and that in comparable cases no appreciable advantage has been observed with the use of interstitial radium.

The use of telecurietherapy, interstitial irradiation, and x-ray irradiation, separately or in combination, is advocated by various observers. Some also support neck dissection in selected cases. Taylor and Nathanson (11) postulate that neck dissection is indicated when lymph node metastasis follows an apparent complete regression of a primary tumor which had previously displayed no evidence of such metastatic involvement. The question therefore arises as to whether any single procedure, or even several procedures, can offer increased life expectancy to the patient with a malignant tonsillar tumor beyond that afforded by x-ray alone. Since each case must be considered individually, no comprehensive statement would be valid. In isolated instances, in which a cervical node has appeared following adequate control of the primary lesion that had not previously metastasized, subsequent surgical or interstitial treatment may be required. In general, however, the results of x-ray treatment alone have been as satisfactory as those from any other single procedure or from a combination of several.

Unfortunately, in many cases the disease is so advanced that only palliative treat-

ment is feasible. The age of the patient (34 per cent of the present group were over seventy years old) frequently prevents the employment of as intensive doses of radiation as might otherwise be indicated. Palliative therapy occasionally adds several comfortable months of life and consequently is to be encouraged even though the prognosis is apparently hopeless. Carcinoma in an advanced stage may in rare instances respond in an unexpectedly favorable manner, both the primary tumor and the metastatic nodes grossly disappearing.

Because certain tumors prove to be unusually radiosensitive, it does not follow that they should receive less than the maximum tolerated dose of radiation. On the other hand, over-irradiation must be guarded against. In attempting to control extensively infiltrating cancer (often complicated by infection), necrosis, slough, and fistula formation may occur after even minor doses of radiation.

SUMMARY AND CONCLUSIONS

1. Ninety unselected cases of cancer of the tonsil treated by irradiation have been presented. The five-year survival rate of 15 per cent is comparable to, but has not surpassed, results generally reported. The results of palliative therapy have been very satisfactory.

2. From the evidence presented, the grade of the lesion has not proved to be of great prognostic significance, except that tumors of low grade were controlled with difficulty. Lympho-epitheliomas appeared to respond well and have warranted in this small group a less guarded prognosis than other types of tonsillar cancer. This may be due to the fact that their rapid growth leads the patients to seek treatment before remote metastases have developed.

3. The presence of metastases necessitates a guarded prognosis in respect to five-year survival, but it should not discourage the use of intensive irradiation, since a certain number of patients respond well to treatment.

4. As compared with treatment without radium, interstitial radium insertion has produced no noticeable improvement in results. External irradiation, adequately given, seems to be the treatment of choice in most cases of carcinoma of the tonsil.

5. In the group studied, supervoltage irradiation has produced a significant increase in the percentage of five-year survivals as compared with high-voltage therapy.

Mason Clinic
Seattle 1 Wash

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SUMARIO

Tratamiento del Cáncer de las Amígdalas

Preséntanse 90 casos, sin seleccionar, de cáncer amigdalino tratados con la irra-

diación (roentgenoterapia de supervoltaje o alto voltaje, con radio por vía intersticial

TABLE IV TUMORS OF THE TONSIL COMPARISON OF RESULTS OF SUPERVOLTAGE AND HIGH VOLTAGE TREATMENT

Years Survived	Supervoltage Radiation			High Voltage Radiation		
	No with Opportunity to Survive	Survived		No with Opportunity to Survive	Survived	
		No	Per Cent		No	Per Cent
1*	36	21	58			
2	30	13	43	43	21	49
3	28	9	32	36	13	36
4	26	6	23	28	5	18
5	21	5	24	23	3	13
				18	1	6

* Eleven patients treated during 1945 are excluded from this analysis

after the initial treatment, supplemental treatment appeared to be of definite value.

Comparison of Supervoltage and High Voltage Treatment Because of reports from other clinics of the great advantage offered by supervoltage as compared to lower-voltage treatment, especial interest was taken in comparing the results of these two methods of irradiation. Of the entire group, 50 patients were treated with high-voltage and 40 with supervoltage radiation. Table IV shows the survival rates in the two groups. Over the ten-year period, for patients having the opportunity to live five years, the percentage of survival was 24 in the group treated with supervoltage and 6 in those receiving high-voltage therapy. The difference between these figures is significant but, in evaluating them, other factors should be borne in mind. First, the number of cases in each group is not large. Second, a division of the ten-year period into two five-year periods showed that, while in the first five years, the survival rate with supervoltage was more favorable than that with high voltage, in the second period the results were roughly comparable. This shift in values is due primarily to a gradual improvement in the method of treatment with high-voltage radiation. Holmes and Schulz (4) report a five-year survival rate with supervoltage therapy of 21 per cent and conclude that this form of irradiation warrants further trial in carcinoma of the tonsil.

DISCUSSION

In the relatively few large series of carcinoma of the tonsil published in recent

years (1, 3, 5, 6, 7, 9, 10), the five year survival rates, ranging from 10 to 17 per cent, are comparable with the 15 per cent rate in the present group. It is significant, however, that in this series almost equally satisfactory results have been obtained without supplementary surgical procedures, and that in comparable cases no appreciable advantage has been observed with the use of interstitial radium.

The use of telecurietherapy, interstitial irradiation, and x-ray irradiation, separately or in combination, is advocated by various observers. Some also support neck dissection in selected cases. Taylor and Nathanson (11) postulate that neck dissection is indicated when lymph node metastasis follows an apparent complete regression of a primary tumor which had previously displayed no evidence of such metastatic involvement. The question therefore arises as to whether any single procedure, or even several procedures, can offer increased life expectancy to the patient with a malignant tonsillar tumor beyond that afforded by x-ray alone. Since each case must be considered individually, no comprehensive statement would be valid. In isolated instances, in which a cervical node has appeared following adequate control of the primary lesion that had not previously metastasized, subsequent surgical or interstitial treatment may be required. In general however, the results of x-ray treatment alone have been as satisfactory as those from any other single procedure or from a combination of several.

Unfortunately, in many cases the disease is so advanced that only palliative treat-

Gout Clinical, Pathologic and Roentgenographic Observations

EDWARD F. ROSENBERG, M.D.,² and ROBERT A. ARENS, M.D.³

Chicago, Ill

WHILE IT IS true that gout often goes undiagnosed and much needs to be done toward educating American physicians to recognize this disease, nevertheless progress has been made. This progress has had a distinct bearing on roentgenology, for important developments in the clinical and pathological fields have greatly improved our ability to interpret roentgenographic findings in patients with this disease. In this paper, we shall outline briefly some historical features regarding roentgenography in gout. We shall also describe some significant developments concerning clinical and pathologic aspects of gout and relate these to the principles of roentgenology which are pertinent to the diagnosis of this condition.

HISTORICAL

The use of the roentgen rays as an aid in the diagnosis of gout was first reported by Huber (1). That writer, in 1896, published a reproduction of a roentgenogram which illustrated the lesions produced by gout in one case. Circular zones of translucency in the subchondral bone were demonstrated and their probable relationship to the deposition of urates in the affected tissues was discussed. Hypertrophic spurs, partial or complete destruction of some joints, and subluxations were described.

A very large number of publications have, since that time, referred to the roentgenographic phenomena associated with gout. This literature is not reviewed here in detail. It seems appropriate, however, to mention the contributions of a few outstanding writers.

Points of distinction between the roent-

gen changes which are to be seen in gout and those encountered in patients with rheumatoid arthritis were described in 1905 by Strangeways and Burt (2). Their observations were based upon a comparison of roentgenograms from a hundred gouty and a hundred rheumatoid patients. Findings which were described as characteristic of gout included increased density of bone, bony additions about joints, nodes on the shafts of phalanges, spurs about the heads of the long bones, loss of cartilage, erosion of bone, transparent areas, and dislocations. There were some instances of complete disorganization of bones and even of bony ankylosis.

Strangeways and Burt conducted this study with great thoroughness but unfortunately omitted a correlation of roentgenographic findings with the clinical aspects of the cases. As a result, roentgenographic changes which they encountered in advanced stages of gout were subsequently considered characteristic of all gouty joints.

It remained for Jacobsohn (3) to point out, in 1913, that roentgenograms should not be relied upon to distinguish gout from other forms of arthritis in every instance. In some cases of gout he found changes which closely resembled those encountered in other diseases of joints, but in certain instances lesions which are not to be seen in any other form of joint disease, notably semicircular or oval zones of destruction irregularly disposed about affected joints, were present. Jacobsohn also described cases in which the lesions produced by gout resembled enchondromas and noted the shadows which are cast by subcutaneous tophaceous deposits.

Interesting American studies of the

¹ Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1940.

² Chief of the Arthritis Clinic, Michael Reese Hospital, Chicago.

³ Director of the X-ray Department, Michael Reese Hospital, Chicago.

en algunos casos) El coeficiente de 15 por ciento de sobrevivencias de cinco años es comparable con los resultados comunicados generalmente, pero no los supera. El resultado de la terapéutica paliativa ha sido muy satisfactorio.

A juzgar por los datos presentados, el grado de la lesión no tuvo mayor importancia en el pronóstico, salvo en que los tumores de grado bajo fueron cohibidos con dificultad. Los linfocarcinomas aparentemente respondieron bien y justifican, en lo relativo a este pequeño grupo, un pronóstico menos reservado que en otras formas de cáncer de las amígdalas, quizás debido a que su rápido desarrollo hace que los enfermos busquen tratamiento antes de presentarse metástasis remotas.

La presencia de metástasis impone un pronóstico reservado con respecto a sobrevivencias de cinco años, pero no debe desalentar el empleo de la irradiación intensa, dado que cierto número de enfermos responden bien al tratamiento.

Comparado con el tratamiento sin radio, la introducción intersticial de radio no mejoró mayor cosa el resultado. La irradiación externa, adecuadamente administrada, parece ser el tratamiento de elección en la mayor parte de los casos de carcinoma amigdalino.

En el grupo estudiado, la irradiación de supervoltaje, comparada con la de alto voltaje, logró un aumento significativo en el porcentaje de sobrevivencias de cinco años.



period Subcutaneous tophi may assume huge proportions and by centrifugal growth may destroy the overlying integument, producing sinuses which discharge crystalline urates and also necrotic matter The sinuses may become infected, after which repeated healing and opening may be observed Even at this late stage, hyperuricemia is not a constant feature of the disease

THE PATHOLOGIC PHYSIOLOGY OF GOUT

Gout appears most likely to be the result of a disturbance in the chemical mechanisms by which the body handles and disposes of uric acid This has been evident for nearly a century and a half, since Wollaston demonstrated urates in tophaceous material in 1779 The exact nature of the anomalous uric acid metabolism is, however, not yet clearly understood Proof is lacking that the gouty patient is deficient in ability to excrete or to destroy urates No decisive evidence has been found to indicate that these persons produce more uric acid than is produced by normal individuals

As no more promising direction has been suggested for such studies, researches regarding the metabolic defect will necessarily continue to explore the field of urate metabolism in a search for a solution to this mysterious feature of gout

PATHOLOGY OF GOUT

A unique and specific lesion, the gouty granuloma, is characteristically present in tissues affected by gout The histologic features of the lesion are fundamentally similar in such different sites as the cartilages of the ear, the olecranon bursae, the kidney parenchyma, and various parts of affected joints Similar lesions have occasionally been observed in the tongue, the myocardium, and even in the valves of the heart This pathognomonic lesion is readily discernible in properly prepared histologic specimens

The gouty granuloma consists of three regions (a) a central zone, in which are deposited crystalline urates cholesterol,

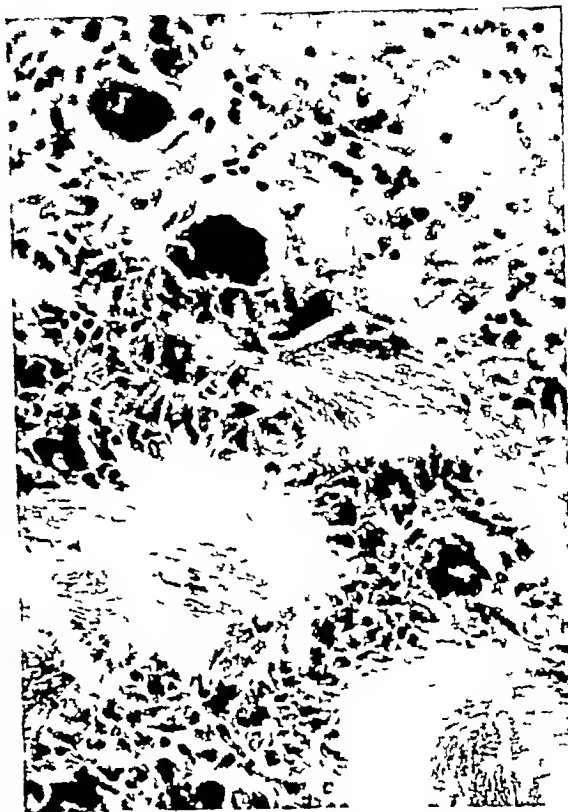


Fig 1 Gouty granuloma showing necrotic central zones surrounded by inflammatory cellular layer A number of giant urophages are present $\times 145$

and debris of necrotic tissue, (b) surrounding this central zone of caseation and crystals, an inflammatory region of varying cellularity, (c) beyond this, a stroma or supporting tissue of varying fibrous density (Fig 1)

The inflammatory cellular layer adjoining the central zone resembles the cellular layer which may be seen about the necrotic centers of true tubercles, consisting of reticulo-endothelial cells, lymphocytes, and plasma cells The cellular content of these lesions differs from that of tubercles, however, by the presence of giant reticulo-endothelial cells, some of which incorporate huge numbers of nuclei in a single protoplasmic agglomeration Some of these cells ingest bundles of urate crystals or incorporate them in the cytoplasm Because of this phenomenon, these giant cells have been called "urophages"

The histogenesis of the gouty tubercle is

roentgenographic phenomena associated with gout were reported in 1919 by McClure (4) and in 1920 by McCarty (5). The presence of focal areas of decreased density was the only change present in some cases. Variable degrees of osteoporosis, narrowing of joint spaces, and bony proliferations were noted. No definite relationship between the duration of the symptoms and the character of the roentgenographic changes was observed.

Upon these foundations, and upon the observations which have been reported in many additional worth-while papers, a more complete and more useful concept of the place of roentgenograms in the diagnosis of gout may now be constructed.

THE LIFE HISTORY OF GOUT

Knowledge relative to the clinical course of gout has been greatly advanced in recent years. Many of the vague, outmoded notions which were handed down to us from previous centuries have been discarded as the life history of this disease has been more clearly outlined.

It is now evident that the symptoms of gout generally progress in an orderly and developing pattern, which may be considered as including (a) a larval period, (b) a period of acute articular attacks, and (c) a period of chronic articular gout, occurring in that order.

The larval period, which is of varying duration, precedes the clinical evidence of articular involvement. Since the specific pattern of disordered chemistry which constitutes the basic anomaly of gout is either inherited or develops very early in life, the larval period may date from birth. During this period gout is usually asymptomatic, although there may be attacks of renal colic as a result of the passage of calculi. The level of blood uric acid may be elevated, and rarely one may find subcutaneous tophi.

The advent of articular attacks should be considered as marking the opening of the second period of gout. These attacks, which characteristically have their onset in the third to the sixth decade, are acute,

self-limited, and of varying intensity. They tend to appear without premonition and often affect a bunion joint primarily. Involvement of the bunion joint is not by any means a regular feature of the early attacks, however, as almost any of the joints of the extremities save shoulders and hips may be the initial site.

The onset is occasionally nocturnal but may occur during the day. Early attacks generally remain monarticular, but a series of two or more joints may be affected. Pain is variable, being moderate in some and violent in other instances. Early attacks usually subside within a few days, or at most within a few weeks, although there is a tendency for the attacks to be more prolonged as their number increases.

If the patient is not treated effectively, attacks may recur at intervals of months or years during the second period, tending to involve additional joints.

Hyperuricemia is more frequently encountered during the second period than during the larval period but is not constant during this or during any of the periods of gout. Tophi are encountered with increasing frequency after the onset of the articular attacks. Renal colics may occur in the second period and there is also a notable tendency to episodes of olecranon bursitis.

In persons who have had numerous and prolonged articular attacks, non-remitting joint deformities may appear, marking the advent of the third and final period of gout. Once developed, these deformities persist until death unless corrected surgically. In some cases, serious crippling may result, and further acute inflammatory episodes may also be observed in the chronically deformed joints.

Chronic deformities of the third period of gout are often typical in appearance, being markedly asymmetric. In some instances, however, these are symmetric and may resemble somewhat the deformities produced by chronic rheumatoid arthritis.

Chronic nephritis, recurring renal colics, and extensive deposits of tophaceous material may be encountered during the third

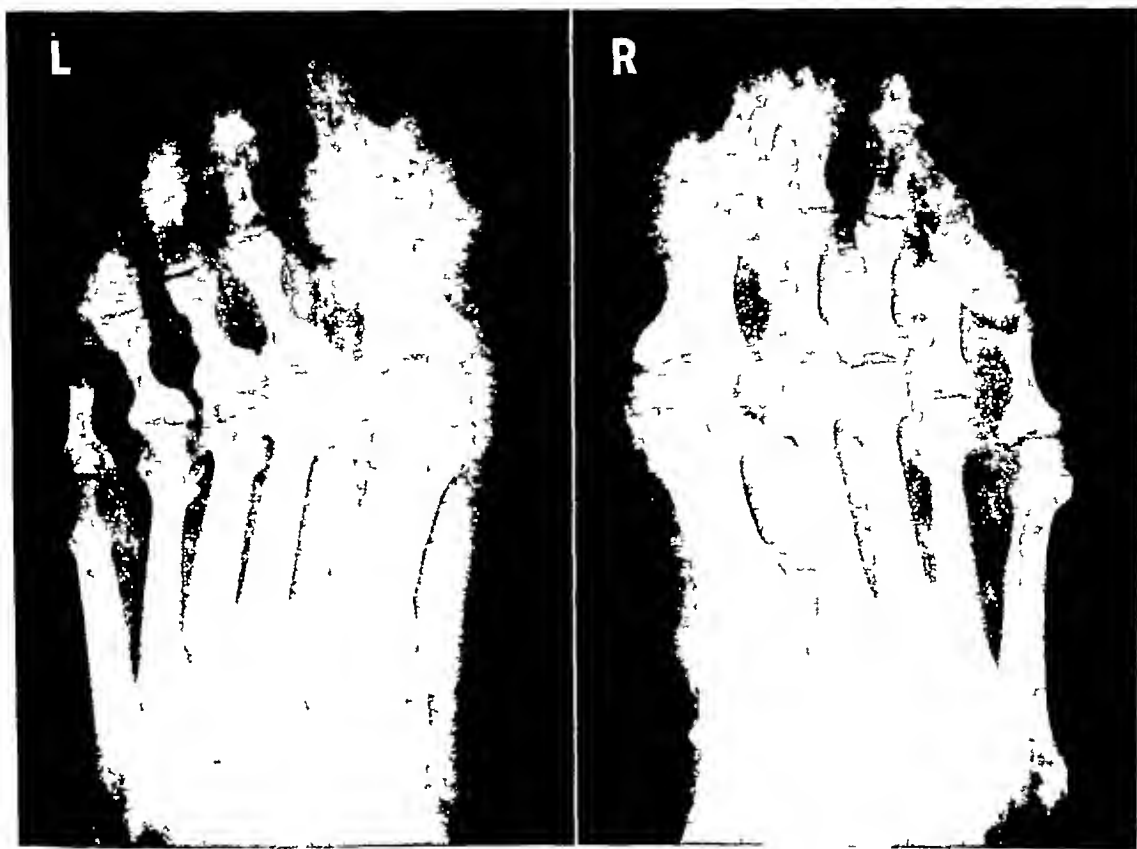


Fig 4 Narrowing of the joint space is present at the interphalangeal joint of the right great toe. This joint also shows marginal hypertrophy and semicircular and circular translucencies. Destructive lesions are more advanced in the interphalangeal joints of the first toes than in the metatarsophalangeal joints.

state of advancement of the pathologic changes which have been described above. Although pathologic changes do not always exactly parallel the clinical stage of the disease, gross parallelism is usually evident.

In every series one must expect to find a considerable number in whom roentgenograms of joints previously affected by gouty attacks are negative. Such negative roentgenograms will be found in cases in which the pathologic lesions are slight, usually in persons who have had few attacks.

The speed of progression of the pathologic lesions is widely variable in different individuals, and a corresponding wide variability is encountered in the roentgenographic observations in different cases. Some persons in the second period have recurrences of acute articular attacks only at long intervals of years or decades. In

these cases, pathologic developments are long delayed, and roentgenographic changes are slow to appear. In other instances the disease runs a more virulent or malignant course. Such patients suffer from a large number of attacks within a few years, have rapidly developing pathologic lesions, and enter the third period, with its articular destruction and larger subcutaneous and articular deposits of urates, relatively early.

The earliest roentgen evidence of changes resulting from gout is not to be expected until fairly late in the second period and should be looked for in the bunion joint. The first notable change is the appearance of a zone of osteoporosis on the medial aspect of the base of the first metatarsal bone and first phalanx (Fig 2).

As the gouty process becomes more extensive, this zone of osteoporosis becomes



Fig 2 A zone of osteoporosis on the medial aspect of the base of the first metatarsal bone and first phalanx is the earliest roentgen evidence of gout

Fig 3 A cystic lesion in the head of the metatarsal bone

apparently as follows. The crystals are deposited first. Evidently, these are quite toxic and cause the death of adjoining cells. Degeneration and necrosis then ensue to produce the central caseous-crystalline zone. The presence of this necrotic material brings forth a foreign-body reaction in the surrounding tissues, thus producing the cellular layer. An attempt occurs to wall off this zone of inflammation by means of fibrous tissue, and the resulting fibrosis constitutes the third or supporting layer.

The synovial membrane reacts to the presence of gouty tubercles by thickening and pannus formation. In location and general form, this pannus does not differ from that to be observed in rheumatoid and tuberculous arthritis, but gouty pannus is distinctively encrusted with urates. It may cover the entire cartilaginous surface of a joint and give to the interior an appearance of having been smeared with coarse white paint.

Gouty tubercles form also in the osseous tissues at the ends of bones. These may expand by centrifugal growth, join with the tophi of the synovial membrane, and bring about a more or less complete destruction of the joint.

Similar lesions form in the capsules of joints. Here the tubercles cause a thickening and loss of pliability. This capsular thickening is to some extent responsible for the deformity and loss of mobility which one encounters in chronic gouty arthritis. When gouty tubercles form in kidneys, the resulting foreign-body reaction destroys the normal architectural arrangement of the kidney and brings about the diseased state which may be designated gouty nephritis. In bursae, thickening and fibrosis are produced.

ROENTGENOGRAPHIC OBSERVATIONS

The roentgenographic findings in a patient with gout are dependent upon the

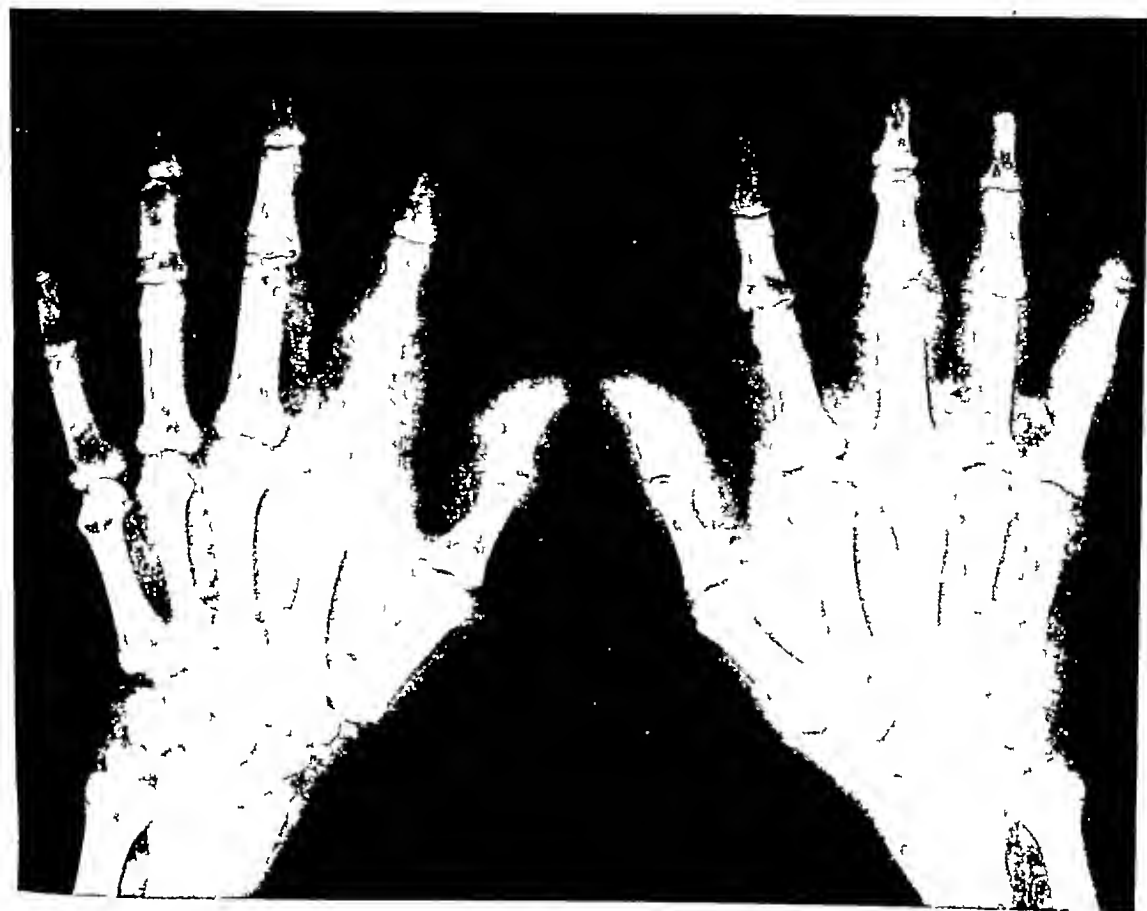


Fig 7 Expansion of the cortex of bones produced by tophaceous deposits. These lesions may resemble the expansile lesions observed in certain tumors of bone

of misdiagnosis, patients are kept immobile in bed for exceptionally long periods. The effects of the acute localized inflammation and disuse may then bring about widespread atrophy. There may be no other evidence of gouty destruction, so that atrophy of bone may be the only visible roentgenographic abnormality.

When the roentgenologist encounters patients with joint disease associated with amputation of some portion of an extremity, the diagnosis of gout should be recalled. Amputations are occasionally required in this disease because of the presence of stubborn draining sinuses or seriously crippling deformities which interfere with the proper use of an extremity.

Tophi have been referred to as 'chalk stones' because of the white, chalky ap-

pearance of their contents. This material does not contain notable quantities of calcium, and tophi are consequently not particularly radiopaque. In consequence of this, larger tophaceous masses cast only evenly dense roentgenographic shadows, the opacity of which will be dependent upon the size of the tophaceous mass (Figs 6 and 8). Smaller tophi cast no shadows whatever.

The renal calculi which are encountered in gouty individuals consist largely of agglomerations of ammonium urate crystals. These uratic stones are relatively small, ranging in size from 1 to 3 or 4 mm in diameter. Such stones are not radiopaque and, because of their small size, they do not produce filling defects which can be detected in the average urograms.

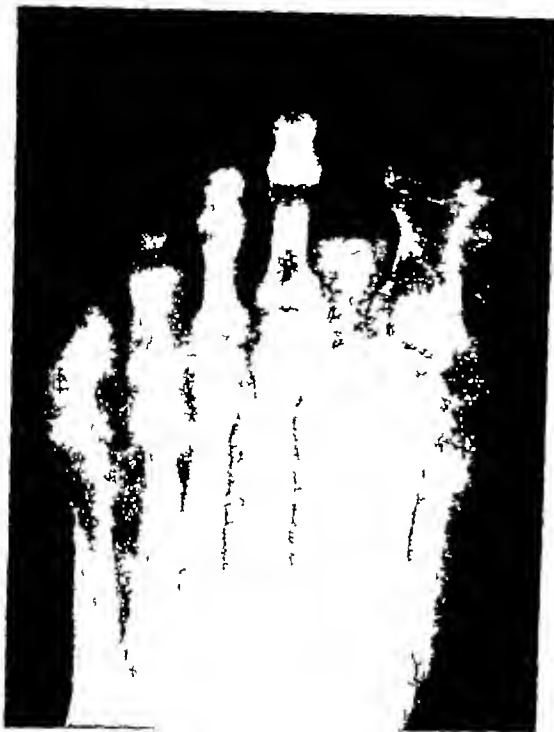


Fig 5 Extensive destruction of the metatarsophalangeal joint. The numerous areas of cystic caries produce a honeycomb effect.

frankly cystic. At the sites of such lesions, the bony structure is completely obliterated and roentgenograms consequently show a "punched out" appearance (Fig 3).

The next stage of gouty destruction results in narrowing of the joint spaces as a result of erosion and obliteration of cartilages by the gouty pannus. Because this process is uneven, surfaces of joints sometimes become markedly irregular. Continued use of such joints produces traumatic effects, as a result of which marginal hypertrophic changes appear (Fig 4).

An even more destructive effect may be seen where tophaceous deposits in the ends of bones expand greatly. These lesions may cause widespread obliteration of the epiphyses and joints (Fig 5). Entire joints may disappear at such sites leaving bony stumps projecting into a formless tophaceous mass (Fig 6). In some advanced instances, one sees the results of combined processes, including erosions, marginal proliferations, and fractures of remaining shreds of bone structure.

An occasional result of large uratic deposits in epiphyseal regions is expansion of the cortex of bones (Fig 7). This may produce an appearance in the roentgenograms resembling somewhat the picture seen when certain tumors of bone produce expansile effects, *e g*, giant-cell tumors or osteogenic sarcomas.



Fig 6 The entire joint between the first and second phalanges of the fifth finger has disappeared, leaving the bony stumps projecting into the tophaceous mass.

Negative roentgenograms of joints do not necessarily exclude the presence of gouty lesions. If pannus formation predominates and if this process is not accompanied by invasion of the epiphyseal bone by gouty lesions, fairly extensive pathologic lesions may be present in joints which cast no abnormal shadows.

In a joint which has been the site of an acute attack of gouty arthritis, osteoporosis may appear very rapidly. This is especially apt to be observed when, as a result

SUMARIO

La Gota

Es de esperar que la naturaleza de las alteraciones radiográficas observadas en los gotosos reflejen las características clínicas y patológicas evolutivas de dicha enfermedad. Para la debida interpretación de esas alteraciones radiográficas resulta indispensable conocer la biología de la gota y las alteraciones patológicas vinculadas con dicho estado. La lesión

fundamental producida en los tejidos por la gota consiste en un granuloma único en su género y proveniente de la reacción de los tejidos a los depósitos de cristales uráticos. La aglomeración, fusión y expansión centrífuga de esos tubérculos ocasionan la destrucción y desorganización de los tejidos afectados.





Fig 8 An exceptionally large tophaceous mass in the region of a bunion joint

SUMMARY

The roentgenographic changes which are encountered in patients with gout may be expected to reflect the progressive clinical and pathological features of this disease. For the proper interpretation of these roentgenographic changes, an understanding of the life history of gout and the pathologic changes associated with this condition is essential. The fundamental lesion produced in tissues by gout consists in a unique granuloma resulting from the reaction of tissues to the deposition of uratic crystals. Agglomeration, fusion, and centrifugal expansion of these tubercles bring about the destruction and disorganization of the tissues in which they are found.

104 S Michigan Ave
Chicago 3 Ill

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DISCUSSION

Ray A. Carter, M D (Los Angeles, Calif)

This is an excellent, orderly exposition of gout, and its three stages are logically presented. The two earlier stages which Drs Rosenberg and Arens describe are the ones in which most can be done for the patient and in which we have little or no roentgen evidence. Films are requested to "rule out" gout. The negative film here as in rheumatoid arthritis, is not an innocent thing, because a potentially crippling condition may be progressing in spite of the negative roentgenographic picture. The real roentgen evidence is predominantly of the third stage of gout, a stage of irreparable injury. Even an earlier osteoporosis which the authors displayed had definite associated hypertrophic change in the joint. A secondary osteoarthritis occurs so frequently in these conditions that Hench has said that advanced gout may be indistinguishable from osteoarthritis—logically enough, because secondary arthritis is a part of the picture.

In regard to tophi and calcifications, it is true that most of them, as Dr Rosenberg said, are not radiographically dense. Nevertheless, we do occasionally see sharp, spicular, bundle like densities from which it is difficult to avoid assuming that considerable calcium is present, whatever its origin may be.

Gout may appear much like rheumatoid arthritis. Drs Rosenberg and Arens have displayed a pannus, with its associated destruction of the cartilage, quite analogous to the process occurring in rheumatoid arthritis.

Again I would like to emphasize that this disease should be first diagnosed, if possible, not by the radiologist but from the clinical picture which the authors have so well described.

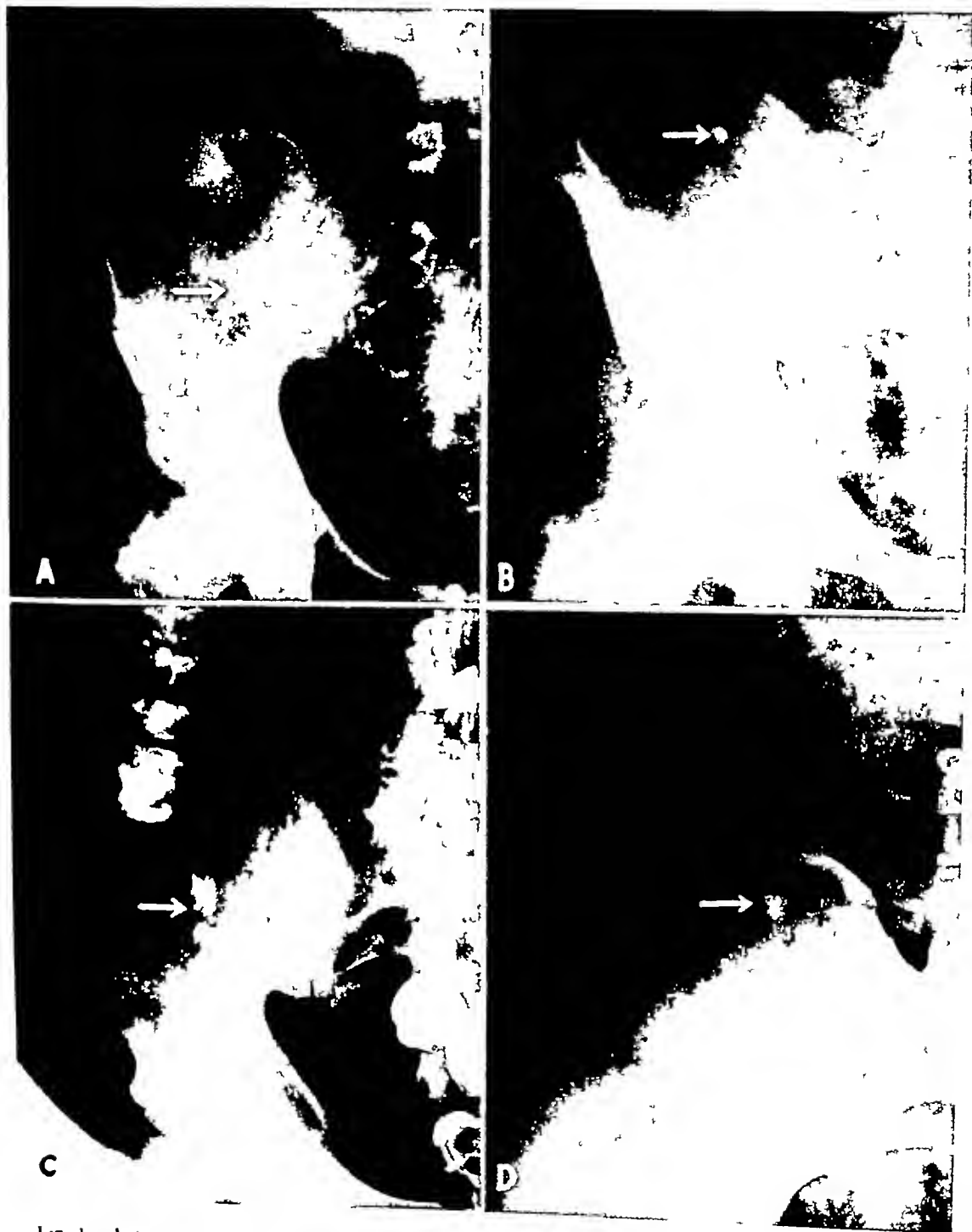


Fig 1 Anteroposterior roentgenograms of right lower quadrant showing appendiceal calculi (arrows) A Case 1 B Case 2 C Case 3 showing three calculi lying inferior and medial to the barium filled cecum D Case 4 In A B and D the reproductions do not show the gas outlined cecum seen on the original films

The Roentgenologic Diagnosis of Appendiceal Calculi¹

BENJAMIN FELSON, M.D.,² and C. MELVIN BERNHARD, M.D.
Cincinnati, Ohio

THE OCCURRENCE of calculi in the appendix has been familiar to surgeons and pathologists for many years, but there is no record of a correct preoperative diagnosis of this condition prior to the use of x-rays. The importance of early diagnosis at once becomes apparent when it is realized that appendiceal calculi usually result in acute appendicitis and that the incidence of perforation in these cases is about 50 per cent.

Weisflog (63), in 1906, contributed the first case report with a correct preoperative diagnosis, demonstrating two calculi in the region of the appendix on a roentgenogram. In a study of 100 cases reported since that time, we have been able to find only 11 more in which the diagnosis was made preoperatively and proved surgically. In an additional 11 instances surgical confirmation was lacking. In 19 patients an incorrect interpretation of the x-ray films was made, and in 13 others the preoperative diagnosis was not clearly stated. In the remainder roentgen studies were not made. In spite of these figures, we believe that the roentgen diagnosis is usually easy to make.

Between June 1943 and June 1946 we encountered 10 patients with appendiceal calculi. Nine of these had roentgen studies from which a diagnosis was made, and 7 of these cases were surgically verified. One patient had no roentgenologic examination, and the diagnosis was first made at operation. During this period, an estimated 300 appendectomies were performed in the various hospitals in which these patients were seen.

This paper is based on 100 cases reported in the literature and the 10 cases from our personal experience, brief histories of which follow.

REVIEW OF CASES

CASE 1 *Acute appendicitis with perforation eight hours after onset, stone in appendix diagnosed radiologically, surgical confirmation, death from acute generalized peritonitis*

C. L., a white male, age 19, was admitted on July 7, 1943, with the history of abdominal pain for eight hours, associated with vomiting. There had been no previous attacks. The temperature was 101° F. Examination was negative except for diffuse rigidity and tenderness in the abdomen, more marked in the right lower quadrant.

Flat and upright films of the abdomen (Fig 1, A), made to rule out perforated peptic ulcer, showed no free air under the diaphragm, but a large, sharply defined, round, laminated, non faceted calculus measuring 1.5 cm in diameter was found lying lateral to the right sacroiliac joint. Stereoscopic views showed the stone in the same plane as the gas filled cecum. A diagnosis of appendiceal stone was made.

The abdomen was explored through a McBurney incision and a perforated appendix with acute generalized peritonitis was found.

Pathologic study of the surgical specimen showed a greatly swollen, acutely inflamed appendix with a bulbous distal half. A perforation was present in the distal third. At this level a hard round stone 1.5 cm in diameter was found (Fig 2, A). It was brown in color and presented two small, somewhat pointed spicules on its surface. Cut sections showed a soft matrix surrounded by concentric laminations. Microscopically there was acute diffuse inflammation of the appendix. Cultures showed *E. coli* and non hemolytic staphylococci. Chemical analysis of the dried stone showed 19 per cent calcium, 13 per cent phosphorus and 14 per cent coprosterol.

The postoperative course was very stormy. The signs of peritonitis persisted, and death occurred on the tenth postoperative day. Autopsy revealed generalized peritonitis, intestinal obstruction due to fibrinous adhesions, two perforations in the distended small bowel, and bilateral lower lobe atelectasis.

CASE 2 *Obscure acute intra-abdominal syndrome, roentgen diagnosis of stone in retrocecal appendix, perforated appendix containing stone found at operation*

J. W., a 21 year-old white male was admitted July 28, 1943, with dull aching pain in the mid

¹ Accepted for publication in December 1946.

² Assistant Professor of Radiology, University of Cincinnati College of Medicine.

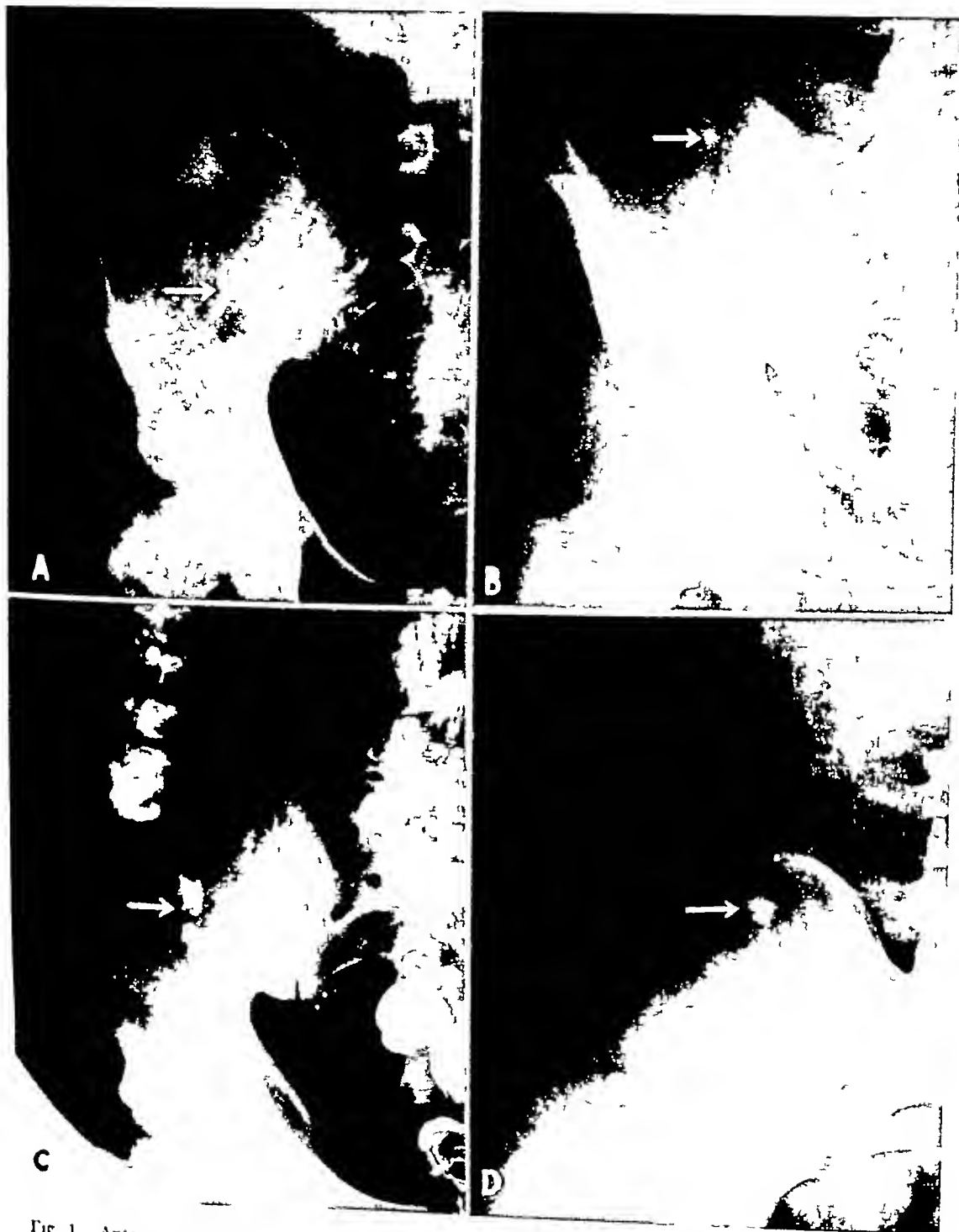


Fig 1 Anteroposterior roentgenograms of right lower quadrant showing appendiceal calculi (arrows) A Case 1 B Case 2 C Case 3 showing three calculi lying inferior and medial to the barium filled cecum. D Case 4 In A B and D the reproductions do not show the gas-outlined cecum seen on the original films

abdomen since the day before, gradually increasing in severity and extending toward the right side. There had been no nausea or vomiting and no symptoms related to the urinary tract. There was no history of previous attacks. The temperature was 100.8° F. Examination was negative except for slight rigidity in the right abdomen with diffuse tenderness over both lower quadrants, more marked on the right. Tenderness was also present in the right costovertebral angle. The white blood cell count was 10,150. Clinical diagnosis was obscure and exploration did not seem warranted because there was no definite localization of symptoms and physical findings. A plain film of the abdomen (Fig 1, B) showed a very faint laminated density, about 4 mm in diameter, in the right lower quadrant. Stereoscopic studies showed this density to be somewhat anterior to the ilium. Immediately anterior to the calculus and extending caudally, a small amount of gas seemed to outline the cecum. The diagnosis of appendiceal calculus was made and, because of the relation between the stone and cecum, a retrocecal appendix was thought to be present.

The abdomen was immediately explored through a McBurney incision. A perforated retrocecal appendix was found. A small amount of yellow cloudy fluid was present in the area, but the surrounding structures appeared normal. The postoperative course was uneventful.

Pathologic examination showed a red, edematous appendix, the serosal surface of which was covered with fibrinopurulent exudate. A perforation was found 1 cm from its tip. There were four calculi present (Fig 2, B). These were soft, smooth, laminated and oval, all lying in the immediate vicinity of the perforation. The largest measured $1 \times 0.6 \times 0.6$ cm and the smallest $0.6 \times 0.3 \times 0.2$ cm. None of the stones was faceted. Microscopically the appendix showed diffuse infiltration of inflammatory cells with some evidence of fibrous changes, and a pathological diagnosis of acute recurrent appendicitis was made. Cultures showed *E. coli*. Chemical analysis of the dried stones showed 21 per cent calcium, 10 per cent phosphorus, and 10 per cent coprosterol.

CASE 3 Acute appendicitis with abscess formation and multiple stones in appendix, correctly diagnosed from clinical and x-ray findings, surgical confirmation

W J S, a 29-year old white male, was admitted on June 22, 1943, complaining of headache and generalized aching for three days, and nausea, vomiting, and diarrhea for one day. There was a slight dysuria, but no abdominal pain. The patient had had no previous attacks. The temperature was 103° F. Examination was essentially negative except for slight distention and resistance across the lower abdomen with generalized abdominal tenderness. Rectal examination was negative. The white blood cell count was 13,850 and

the urine contained 20 to 30 white blood cells per high power field. The stool showed a 4+ test for occult blood. Stool cultures were later reported positive for salmonella organisms, probably of the enteritidis group. Sigmoidoscopy showed a red edematous mucosa with many petechial hemorrhages.

Because of the gastro intestinal symptoms and findings, a barium enema study was done on June 24. It showed localized irritability and spasticity in the sigmoid and slight irritability in the cecum. A density seen medial to the cecum was thought to represent the barium filled terminal ileum.

The following morning, pain developed in the abdomen, more localized in the right lower quadrant, and a definite tender mass was discovered in that region. Appendiceal abscess was suspected and it was decided to wait for better localization before surgical intervention. In the meantime, one of us (B F), recalling the density medial to the cecum, requested that the patient be again examined roentgenographically. Re examination (Fig 1, C) showed the shadow in question to be composed actually of three sharply defined laminated densities, on lateral and stereoscopic anteroposterior views these were shown to be in the same plane as the cecum, which still contained barium. They did not present a faceted appearance. A diagnosis of appendiceal stones was made.

Since the patient seemed to be tolerating the infection poorly, exploration through a right rectus incision was performed on June 25. Marked infection and fibrinopurulent exudate were found, localized to the right lower quadrant. The appendix appeared swollen and injected. A small perforation was present about 6 mm. from the attachment to the cecum. A stone protruded through this perforation. The postoperative course was complicated by a wound infection and by a pelvic abscess, but the patient eventually recovered.

Pathologic examination showed an acutely inflamed appendix 9 cm. long, the proximal diameter measuring 2 cm. and the distal, 0.8 cm. There were five smooth, oval, hard, dark brown stones present (Fig 2, C). The largest measured $1.5 \times 1.0 \times 0.5$ cm and protruded through the perforation, the smallest measured 0.2 cm in diameter. All the stones were laminated but only the four smaller ones were faceted. The cut surfaces were dark brown, somewhat soft, and friable. An acute suppurative appendicitis was found on microscopic examination. Chemical analysis of the dried stones showed 21 per cent calcium, 11 per cent phosphorus, and 8 per cent coprosterol.

CASE 4 Suspected acute appendicitis, stone diagnosed on roentgen examination, surgical confirmation

R B, a 20-year-old white male, was admitted June 30, 1943, with a history of dull aching right lower quadrant pain for two days associated with nausea. There was no history of previous attacks.

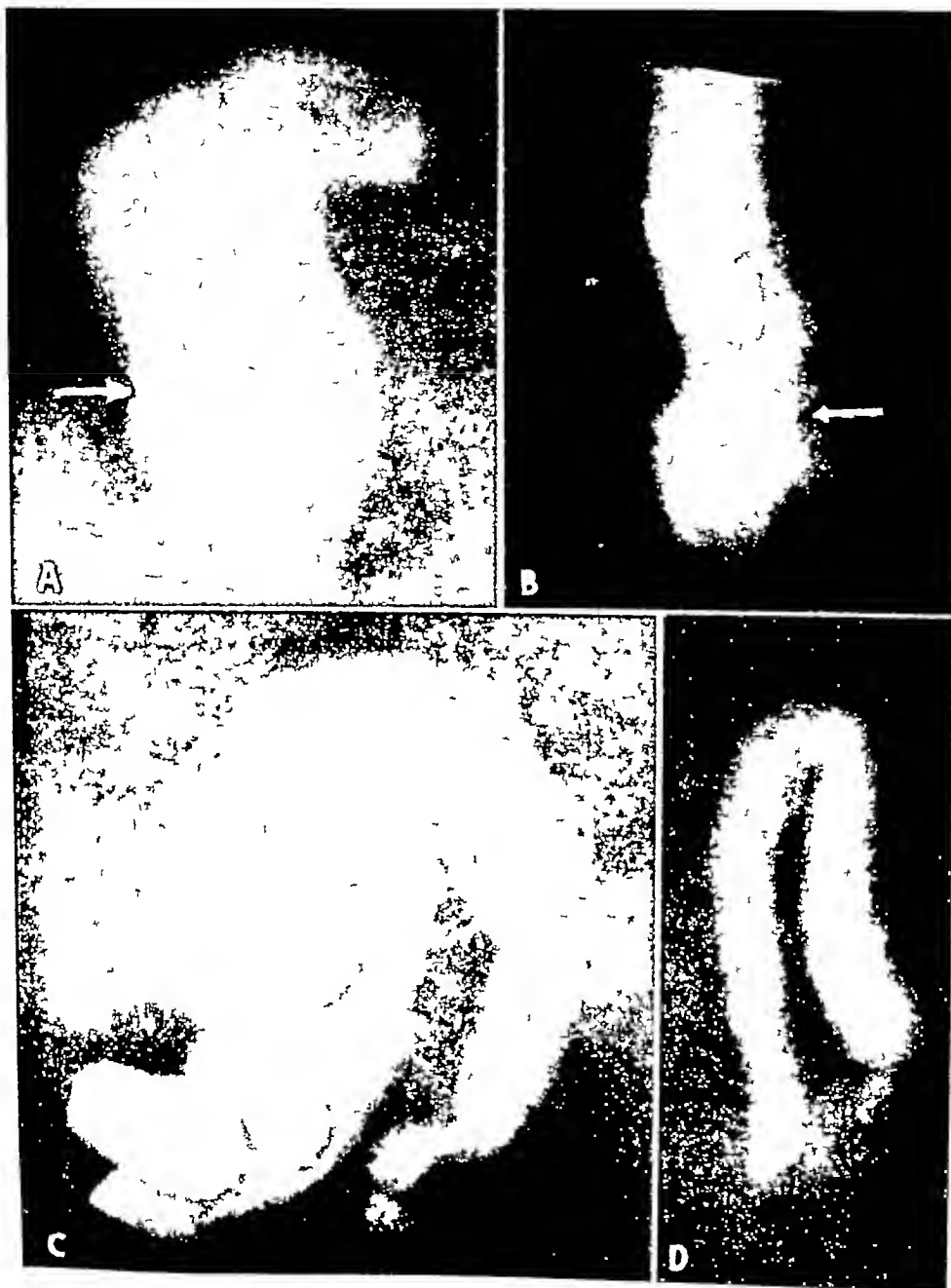


Fig 2 Roentgenograms of appendices removed at operation showing appendiceal calculi *in situ*

A Case 1 Solitary laminated calculus in distal end of greatly swollen appendix Arrow points to site of perforation

B Case 2 Four laminated calculi in distal two thirds of swollen appendix Arrow points to site of perforation

C Case 3 Five laminated and faceted calculi in the proximal third of a swollen appendix. The largest stone protrudes through the perforation Note lesser involvement of the distal appendix

D Case 4 Laminated calculus in distal end of normal sized appendix No perforation



Fig 3 Case 5 Perforated appendix with drainage and appendectomy (?) nineteen years before A Anteroposterior view B Right lateral view C Oblique view following barium enema Calculus (arrows) lies posteriorly and closely related to cecum

The temperature was 97.8°F . Physical examination was negative except for tenderness and slight resistance in the right lower quadrant, and right costovertebral angle tenderness. Rectal examination was negative. The white blood cell count was 8,250 and the urine was normal. Acute appendicitis was suspected. A KUB film of the abdomen (Fig 1, D), made because of the costovertebral angle tenderness, showed a faint, well defined oval density below the level of the crest of the right ilium. It was not faceted. Stereoscopic studies showed the position to be just behind the plane of the cecum, which was outlined by gas and extended about 6 cm below the calculus. It was concluded that an appendiceal stone was present, and from the relation of the stone to the cecum, the appendix was believed to be extending cephalad, in a retrocecal position.

The abdomen was explored through a McBurney incision and the appendix was found to be bound down to the posterior wall of the cecum, pointing upward toward the hepatic flexure.

On pathologic examination the appendix showed a moderate congestion of the serosa. A hard, laminated, non-faceted, dark brown, oval stone measuring 5×7 mm was found in the tip (Fig 2, D). The wall of the appendix was thinner in the region of the calculus than elsewhere. The stone presented a hollow center. Microscopically, the acute reaction was greatest in the region of the stone. In the proximal part of the appendix no inflammatory changes were noted. Some fibrous changes were also observed, and a pathologic diagnosis of acute

recurrent appendicitis was made. The patient recovered without any complications.

CASE 5 Perforated appendix 19 years ago with postoperative draining sinus, no recent symptoms, stone in region of appendix on x ray film, no surgery

K. H., a white male, aged 27, was referred for a gastro intestinal series prior to induction into the Army, because of the history of surgical drainage of a perforated appendix nineteen years earlier. At that time an appendectomy was supposed to have been performed, but no operative note was found in the hospital record. The wound drained for about six months after the operation and ultimately healed. A roentgenogram of the abdomen at that time was reported negative for foreign body. In the interval there had been few symptoms related to the abdomen. Physical examination was entirely negative except for an extensive scarred area in the right lower quadrant.

A plain film of the abdomen (Fig 3, A) preceding the gastro intestinal series showed a sharply defined laminated, oval non faceted shadow, 1.5×1.0 cm in the right lower quadrant at about the level of the iliac crest. Two small spicules projected from its inferior margin. A lateral view (Fig 3 B) showed the density to lie posteriorly. On barium enema study (Fig 3, C) the stone appeared closely related to the posterior wall of the cecum. Both cecum and stone were completely fixed to palpation on fluoroscopic examination.

From the history and roentgenologic findings, it is believed that the appendix may not have been re-

moved at the original operation and contained a calculus, or that one subsequently developed. Another possibility is that the stone was expelled into the peritoneal cavity when the appendix perforated and was present but not recognized on the subsequent roentgenogram of the abdomen

CASE 6 Appendiceal calculus an incidental finding on roentgenographic examination, surgery not performed

D J J, a 25-year old colored soldier, was referred for roentgenograms of the lumbar spine on Oct 16, 1943, prior to his discharge from the Army. He had had a backache following calisthenics three weeks before. The severe pain lasted only one day, but there was a slight persistent aching until a few days before the x-ray examination, when the pain disappeared completely. No other symptoms were noted. There had never been abdominal distress of any kind. Examination was entirely negative except for slight well localized tenderness in the right lower quadrant and slight rectal tenderness on the right.

On the anteroposterior view of the lumbar spine a calcification was found in the right lower quadrant, and further studies, including a barium enema examination (Fig 4), showed it to be a sharply defined, laminated, non-faceted stone constantly related to the medial aspect of the cecum. It was extremely mobile, especially with respiration. It measured 1.5×2 cm. The appendix did not fill with barium.

The patient was discharged from the Army because of an unrelated condition and arrangements were made for his future medical care.

CASE 7 Acute appendicitis, calculus in line of right ureter on roentgenogram, urinary stone ruled out by intravenous pyelography, x ray diagnosis of appendiceal calculus confirmed at operation

J B, white male, aged 19, was admitted Nov 11, 1943, complaining of headache and gradual development of epigastric distress, which later shifted to the right lower quadrant. Nausea began after admission and he vomited once. No urinary symptoms were evident. There had been a similar attack about one year earlier, lasting for two days. The temperature was $98.6^{\circ} F$. Physical examination was negative except for tenderness and slight abdominal rigidity in the epigastrium and right lower quadrant. The rectal examination showed tenderness on the right. The urine revealed a heavy trace of albumin with 8 to 10 red blood cells and 20 to 30 white cells per high power field, with occasional white cell clumping. The white blood count was 16,000, with 52 per cent polymorphonuclears and 46 per cent lymphocytes.

A roentgenogram of the abdomen (Fig 5, A) was made because of the urinary findings and showed a sharply defined laminated calculus in the line of the lower right ureter. An intravenous pyelogram to rule out a ureteral calculus showed the calcifica-



Fig 4 Case 6 Anteroposterior spot film of right lower quadrant following barium enema, showing laminated calculus (arrow) adjacent to medial surface of cecum. No operation.

tion lying medial to the right ureter. A diagnosis of appendiceal calculus was made.

Appendectomy showed an acutely inflamed non-perforated appendix, which lay inferior and medial to the cecum.

Pathologic examination showed a markedly congested serosa covered with fibrinopurulent exudate. A single, hard, laminated, oval calculus (Fig 5, B), $1 \times 0.6 \times 0.6$ cm, was found in the proximal third of the appendix. It was not faceted. Microscopic examination showed a diffuse acute appendicitis. Recovery was uneventful.

CASE 8 Obscure abdominal symptoms and backache, roentgenologic diagnosis of calculus in retrocecal appendix, surgical confirmation, complete relief of symptoms

A white soldier, aged 39, was admitted to a field hospital June 15, 1945, because of low back pain. Since June 1944 he had had three attacks of pain in the epigastrium and one attack of lower right quadrant pain. These attacks lasted for two to fourteen days each and were associated with vomiting. Between attacks and on admission there was constant vague epigastric distress, worse after meals, with occasional vomiting. The back pain began about one month before admission and was fairly constant and of varying severity. It was not related to exercise or position.

On admission to the field hospital, the physical examination was completely negative. There was no abdominal tenderness. The temperature was



Fig 5 Case 7 A Anteroposterior view of the pelvis shows a laminated calculus (arrow) in the line of the right lower ureter. An intravenous pyelogram showed the calculus medial to the ureter. B Roentgenogram of the appendix after removal showing the calculus in the proximal third of the slightly swollen organ. No perforation.



Fig 6 Case 8 A Anteroposterior view of abdomen showing laminated calculus above right iliac crest. B Lateral view showing calculus (arrow) lying far posteriorly in abdomen. Inset Roentgenogram of calculus showing laminations.

normal. Roentgenograms of the lumbar spine were negative except for a round laminated calcification, 1.75 cm in diameter, in the posterior portion of the right lower quadrant, 3 cm above the iliac crest. A gallbladder series showed a normal functioning gallbladder lying well above the calculus. Follow-

ing a laxative moderate abdominal pain developed, the temperature rose to 99.6°, and there was mild lower abdominal tenderness. These symptoms subsided after thirty-six hours.

The patient was transferred to a general hospital for further study. On admission he still complained



Fig 7 Case 9 Roentgenogram of laminated calculus found in appendiceal abscess

of epigastric distress and mid-line back pain. His white cell count was normal, but his temperature occasionally rose to 99.4° . A clinical diagnosis could not be made, although duodenal ulcer was suspected. On reviewing the films (Fig 6), a diagnosis of appendiceal calculus was thought likely. In the absence of fever and leukocytosis, it was considered safe to do a barium enema study. This showed the calculus closely related to the postero-medial wall of the cecum. It moved slightly with respiration but was immobile to palpation. Over it there was slight tenderness to pressure. A diagnosis of a calculus in a retrocecal appendix was made.

At operation the appendix was found adherent to the posterior wall of the cecum, the tip pointing upward. The cecum maintained a relatively high position. The appendix was removed with difficulty. It was 4 cm long. About 0.5 cm distal to its cecal attachment was a large circular swelling. Distal to this swelling the appendix narrowed abruptly.

On opening the appendix, a large smooth, brownish green spherical calculus was found (Fig 6, inset). It measured 1.5 cm in diameter. On section it showed concentric laminations. Proximal to the stone the mucosa of the appendix was normal. In the dilated portion of the appendix the mucosa presented a granular, injected appearance. Distal to the stone the mucosa appeared normal. Microscopic sections showed moderate acute appendicitis.

The postoperative course was uneventful and all the symptoms disappeared. One month later the patient was discharged to duty.

CASE 9 *Clinical diagnosis of appendiceal abscess, no roentgenograms, operation showed ruptured appendix with calculus in abscess cavity*

G S, a 20 year old German prisoner-of-war, was admitted July 21, 1945, with a history of diarrhea for three weeks, followed by generalized abdominal pain which subsequently localized in the right lower quadrant and persisted. He had had vague abdominal pain for some time preceding this attack. Examination on admission revealed no spasm or rigidity but a tender mass was felt in the right lower quadrant. Urine was negative, the white blood



Fig 8 Case 10 Anteroposterior view of abdomen showing laminated calculus (arrow). Inset Roentgenogram of appendix after removal, showing three laminated calculi

count was 10,500 and the sedimentation rate was 32. No roentgenograms were made.

The appendix was not found at operation, but there was a small hole in the base of the cecum. An appendiceal abscess containing 3 cc of pus and a calculus, was present. The calculus was non-faceted, firm, dark brown, cylindrical in shape, and measured $1.2 \times 0.4 \times 0.4$ cm. Its cut surface was laminated (Fig 7).

The patient made an uneventful recovery.

CASE 10 *Clinical diagnosis of ureteral stone, roentgen diagnosis of calculus in retrocecal appendix, acute retrocecal appendicitis with calculi found at operation*

R L, a 24 year-old white male, was admitted to the Cincinnati General Hospital on Aug 20, 1946, because of severe constant right flank and right lower quadrant pain beginning seven hours before admission. Pain was accompanied by nausea and one liquid stool.

For the past three years the patient had suffered intermittent bouts of mild abdominal pain lasting up to fifteen minutes, usually periumbilical and in the right lower quadrant, not associated with nausea or vomiting. During the week preceding admission

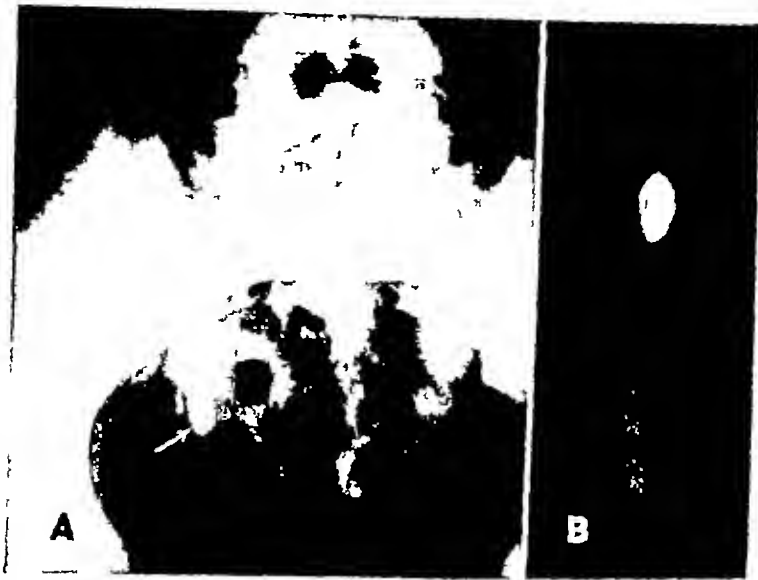


Fig 5 Case 7 A Anteroposterior view of the pelvis shows a laminated calculus (arrow) in the lumen of the right lower ureter. An intravenous pyelogram showed the calculus medial to the ureter. B Roentgenogram of the appendix after removal showing the calculus in the proximal third of the slightly swollen organ. No perforation.

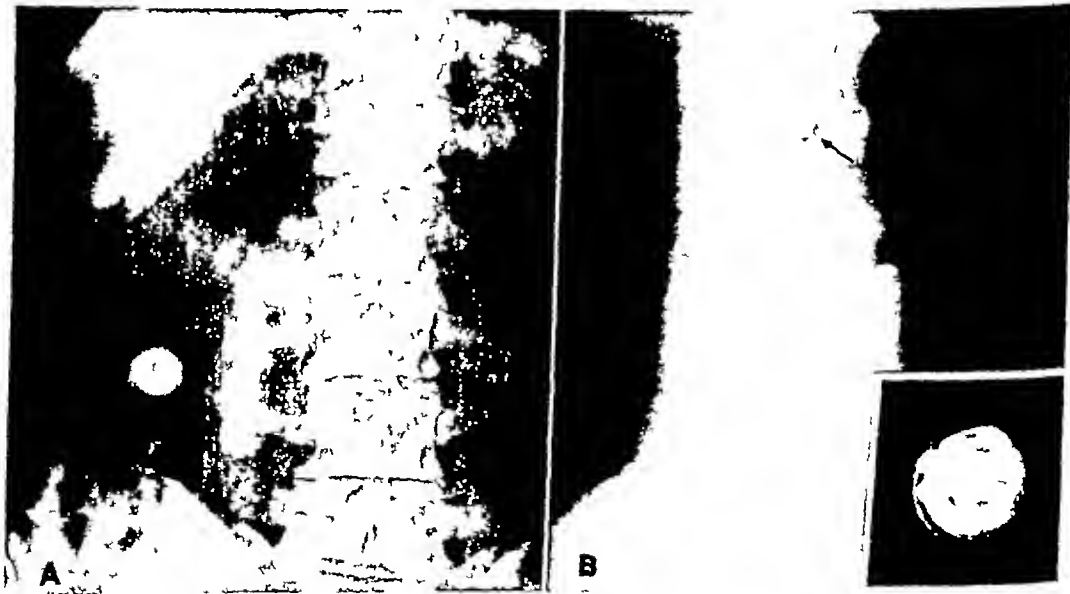


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normal. Roentgenograms of the lumbar spine were negative except for a round laminated calcification 1.75 cm in diameter, in the posterior portion of the right lower quadrant, 3 cm above the iliac crest. A gallbladder series showed a normal functioning gallbladder lying well above the calculus. Follow-

ing a laxative, moderate abdominal pain developed, the temperature rose to 99.6°, and there was mild lower abdominal tenderness. These symptoms subsided after thirty-six hours.

The patient was transferred to a general hospital for further study. On admission he still complained

The most plausible and widely accepted explanation of the origin and development of appendiceal stones is that offered by Kelly and Hurdon (31). They state that if the normal return of the fecal contents from the appendix to the cecum by peristalsis is impaired in any way, inspissation of varying degree occurs. The combination of irritation from the fecal mass and bacterial activity produces a low-grade catarrhal inflammation with its attendant secretion of mucus. Inorganic salts contained in the mucus are precipitated (probably by bacterial action) on the surface of the dried fecal particle, which thus increases in size. The repetition of this process results in the lamination almost constantly present. Eventually, if some complication does not intervene, the enlarging stone produces pressure atrophy in the secretory glands of the appendix and its growth ceases.

The chemical and microscopic structure of the calculi appears to lend support to this theory. The presence of vegetable fibers in the stones analyzed indicates that fecal material is present (40). Tests for mucus are positive (31). Large masses of bacteria are constantly present.

The next question which arises is the relationship between appendiceal stones and acute appendicitis. From a statistical standpoint there can be little doubt that such a relationship exists. In the entire series of 110 cases, only 5 failed to present clinical or surgical findings of acute appendicitis. The high incidence of perforation also supports this premise.

We believe that in the presence of an appendiceal calculus, obstruction is more complete and distention more marked than in simple acute appendicitis. Consequently perforation is more likely to occur. To support this point of view, we found that in every case in which the relative locations were recorded, the perforation always occurred at or distal to the level of the stone. It is possible that the stone itself erodes through the wall of the inflamed appendix, but from the available evidence this is probably uncommon.

Other less common sources of appendiceal stones have been described. A few instances of typical gallstones containing large amounts of cholesterol, bile salts, and pigment have been reported (31). A foreign body may sometimes form the nucleus of a stone (39, 41). Unaltered foreign bodies in the appendix are not uncommon, but this subject is beyond the scope of our paper. Two instances of pure bismuth stones in the appendix, long after a gastro-intestinal series, have been reported (39, 43).

Clinical Findings Of 60 patients whose sex was stated, 47 were males and 13 females. This preponderance of males conforms to the sex ratio observed in acute appendicitis. The largest number of patients, 21, were in the third decade of life, as compared to 12 in the second and 15 in the fourth.

There are no characteristic symptoms or physical findings which might lead to the diagnosis of appendiceal stone. The diagnosis depends entirely on the roentgen findings. A rather frequent occurrence of urinary symptoms has been reported (39). Recurrent attacks were present in 32 of 52 patients in whom this point was mentioned.

It has been stated (44) that perforation occurs quite early in the course of this disease. In our Case 1, perforation occurred within eight hours, and in Case 2 within twenty-four hours of the onset of symptoms. In the case reports in the literature, the time interval between onset and perforation was seldom clearly stated.

Only 5 patients had no symptoms related to the appendix. In 2 others, stones were present as incidental findings on a previous film, but subsequently acute appendicitis, developed in both, in one with perforation (32, 55).

Roentgenologic Diagnosis When a stone has been demonstrated on a plain film, a variety of procedures have been recommended to localize it. When appendiceal calculus is suspected in acute cases, it has been our policy to obtain immediately lateral and stereoscopic anteroposterior views of the area. These films are viewed wet,

these attacks occurred almost daily, and during this period urgency with nocturia developed.

On admission the temperature was 100° F. There was tenderness to the right of the umbilicus and in the right flank, with rebound tenderness referred to the right lower quadrant.

The white blood cell count was 11,500 and the urine showed 3 to 5 red blood cells per high power field. Because a right ureteral calculus was suspected, a KUB film of the abdomen was obtained (Fig. 8). This showed a laminated calcification measuring 6 × 9 mm lying at the level of the right iliac crest, somewhat laterally. Lateral and stereoscopic anteroposterior views showed the calculus lying just posterior to the ascending colon, about 3 inches above the lower end of the gas-filled cecum. A diagnosis of calculus in the tip of a retrocecal appendix was made.

The patient was immediately explored through a McBurney incision and an acutely inflamed retrocecal appendix closely adherent to the post-cecal wall was found. The tip pointed upward toward the hepatic flexure. Appendectomy was performed with some difficulty.

Pathologic study of the surgical specimen showed an acutely inflamed appendix. The distal end was bulbous and covered with fibrin. No perforation was found. The appendix was 5.5 cm in length, 0.7 cm in diameter at the proximal end, and 1.7 cm in diameter at its distal end. It contained about 2 cc of thick dark brown pus with a fecal odor, and three laminated soft brown calculi (Fig. 8, inset), having the consistency of putty. The largest of these, the only one shown on the KUB film, lay in the bulbous tip and measured 1.3 × 0.6 × 0.6 cm. The center of each calculus was quite soft. The mucosa of the appendix showed small granulations.

The postoperative course was uneventful. The patient has been symptom-free since the operation.

DISCUSSION

Much confusion has arisen in the literature because of the terms ordinarily used to describe appendiceal calculi. They have been variously called fecoliths, stercoliths, coproliths, concretions, enteroliths, stones, and calculi. The first four terms have been applied also, by many authors (21), to the non-calcified inspissated fecal masses so commonly found in the appendix. These are not included in the subject under discussion. The term *enterolith* implies that the stone has developed in the intestine and is identical with the rare calcified intestinal calculus reported under that name (49). This is not the case, as we shall see later. The

term *appendiceal calculus* seems preferable to us, since it implies appendiceal origin of a calcified mass.

Incidence. Bunch and Adcock (7) state that they have encountered only one case of appendiceal stone in over 2,000 patients with appendicitis. Golden (21) remarks that "fecal concretions which contain enough calcium to cast an x-ray shadow must be quite uncommon in this country. I can't remember having seen one." Yet Steinert *et al.* (57) found 10 examples among 104 appendectomies. There have been slightly over a hundred cases reported since 1900, the majority in the foreign literature.

Etiology. There is some difference of opinion regarding the etiology of appendiceal calculi, but most authors now agree that they are generally formed, at least in part, *in situ*. This point of view is supported by the following evidence:

- (1) The majority of stones, being more than 1 cm in diameter, are too large to pass through the cecal orifice of the appendix. Experimentally Guinard (quoted by Calzolari, 8) was unable to force a foreign body the size of a cherry seed into the appendix.
- (2) Kelly and Hurdon (31) report a case in which three small stones were found completely embedded in the appendiceal wall and a larger stone was anchored in the wall by a pointed fang-like process. They quote Ribbert as describing microscopically a continuity between the mucus in the outer layer of a stone and the mucous glands in the appendix.
- (3) The chemical composition of appendiceal stones differs greatly from that of gallstones or true enteroliths.
- (4) Foreign bodies which lodge in the appendix often become encrusted with calcareous material and may even form the nucleus of a typical calculus (41).

The most plausible and widely accepted explanation of the origin and development of appendiceal stones is that offered by Kelly and Hurdon (31). They state that if the normal return of the fecal contents from the appendix to the cecum by peristalsis is impaired in any way, inspissation of varying degree occurs. The combination of irritation from the fecal mass and bacterial activity produces a low-grade catarrhal inflammation with its attendant secretion of mucus. Inorganic salts contained in the mucus are precipitated (probably by bacterial action) on the surface of the dried fecal particle, which thus increases in size. The repetition of this process results in the lamination almost constantly present. Eventually, if some complication does not intervene, the enlarging stone produces pressure atrophy in the secretory glands of the appendix and its growth ceases.

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since perforation, if it has not already occurred, must be considered imminent. The true diagnosis was not suspected in Case 3, and a barium enema was given. We believe the use of a barium enema is inadvisable in acute appendicitis. In 4 of our cases we were able to determine correctly the relationship between the calculi and the gas-filled cecum on stereoscopic films without a contrast medium.

Where the symptoms are not acute, the patient is studied more thoroughly. Genito-urinary, gallbladder, colon and gastrointestinal studies are also made.

Because of the variations in the anatomic position of the appendix, the shadow of the calculus may be found anywhere in the right abdomen, and rarely even on the left side. In all but 5 cases in the literature the stone was in the right lower quadrant, usually at the level of the sacroiliac joint or iliac crest. Twice it was in the right upper quadrant and mistaken for a gallstone. In one patient it was found in the left lower quadrant and correctly diagnosed (16). In a number of instances it was found in the region of the lower right ureter (Case 7), so that pyelography was indicated.

Lamination was demonstrable in nearly all of the patients in whom the x-ray appearance of the calculus was completely described. This finding is of great importance as a diagnostic criterion, since a laminated calculus in the lower right quadrant will almost invariably prove to be an appendiceal stone.

A sharp regular outline was present in practically all the cases. The presence of facets is not uncommon, especially when the stones are multiple, but the demonstration of facets on the roentgenogram is usually difficult.

Of 16 patients to whom barium was administered orally or by enema, 8 showed partial appendiceal filling.

Study of the mobility of the density on fluoroscopic palpation is not very helpful in diagnosis. In 15 patients studied for this finding, 8 showed appreciable mobility while in 7 there was partial or complete

fixation. In Case 6, which was without clinical symptoms, the respiratory excursion of the calculus was quite marked.

When multiple calculi are present, some of the smaller ones may not be visualized on the preoperative films (Cases 2 and 10).

The value of routine roentgenography in acute abdominal conditions receives further support from this study, since this procedure was the chief factor in reaching a correct diagnosis in at least 4 of our 8 cases, permitting a correct and prompt surgical approach.

Differential Diagnosis (1) *Urinary Calculi*. In 10 of the 18 cases incorrectly diagnosed by x-ray examination, the stones were interpreted as urinary calculi. The posteromedial location of the calculi and the absence of lamination favor ureteral calculus. Pyelography may be indicated in the more confusing cases (Case 7).

(2) *Calcified intra-abdominal lymph nodes* are sometimes quite confusing but the wide range of mobility, the dentate borders, the irregular shape, and granular structure of these densities are usually diagnostic.

(3) *Gallstones*. Occasionally, difficulty might arise because of a low-lying gall bladder or high position of the cecum and appendix. Although the x-ray appearance of the two types of stones is often identical, differentiation is usually easy if the cecum is visualized. Gallstone obstruction at the ileocecal valve following spontaneous internal biliary fistula should be readily differentiated by the presence of the symptoms and roentgenologic findings of intestinal obstruction, with perhaps gas outlining the biliary ducts.

(4) *Phleboliths* are seldom a problem because of their characteristic position and configuration, symmetrical distribution, and absence of lamination.

(5) *Foreign bodies* should give no difficulty because of their characteristic shape and density.

(6) *Non-reticulated bone islands in the ilium* are easily located on stereoscopic films.

(7) *True enteroliths in the bowel*. These very rare calculi are said to be larger and

less opaque than appendiceal calculi and surrounded by a thin layer of gas

(8) *Calcifications in epiploic appendages, cysts, tumors, and ligaments* have been mentioned by various authors, but differentiation should not be difficult

In a case recently studied, we suspected an appendiceal calculus because of a triangular calcification anterior to and below the right sacroiliac joint. At surgery an acute appendicitis with perforation and abscess was discovered. The calculus was not found, but a solitary calcific plaque was felt in the right common iliac artery somewhat above the region suspected. It is possible that this accounted for the shadow seen on the film.

Pathology The involved appendix usually shows a diffuse acute appendicitis with areas of gangrene varying in severity and extent, generally more marked at the level of the stone or distal to it. Sometimes evidence of inflammation is slight or entirely lacking proximal to the stone (Case 4).

Perforation occurred in 47 of the 99 patients in whom this complication was mentioned. In 19 cases this resulted in abscess and in 10 in diffuse peritonitis. The type of complication resulting from the perforation was not stated in 18. In 14 patients a calculus either protruded through the perforation or lay adjacent to it, while in 3 the perforation had occurred distal to a calculus. In no instance was the perforation found proximal to the calculus. In 12 patients the stone was found completely outside the appendix, having escaped through the perforation. In 18 patients the relative position of the stone and the perforation was not mentioned. The stones occurred with about equal frequency in the proximal, middle, and distal portions of the appendix.

In most of the case reports, the location of the appendix and the presence of kinks, bands, etc., were not mentioned. In 5 of our cases and in 6 reported by others the appendix was in a retrocecal position, usually bound down to the post-cecal wall. This suggests an etiologic relationship; the position of the appendix may interfere

TABLE I APPENDICEAL CALCULI CASES ANALYSIS OF

Number of Calculi	Cases
1	69 (67.6%)
2	13 (12.7%)
3 or more	20 (19.6%)
Size (average diameter)	
Less than 1 cm	29 (41.4%)
1-2 cm	25 (35.7%)
Over 2 cm	16 (22.8%)
Shape	
Oval cylindrical	28 (53.8%)
Round	19 (36.5%)
Triangular	2 (3.8%)
Irregular	3 (5.7%)
Lamination	
Present	34 (94.4%)
Absent	2 (5.5%)
Consistency	
Hard	22 (73.3%)
Soft	8 (26.6%)

with the normal return of fecal contents from the appendix to the cecum and thus initiate the sequence of events postulated by Kelly and Hurdon (31) which culminates in the production of a calculus.

Physical characteristics of the calculi are shown in Table I. Information of this type was lacking in many of the case reports. The largest number of calculi seen in one patient was 23. The largest calculus described was 2.5 cm in diameter and weighed 13.5 gm. Faceted calculi were described in only 8 cases, in 4 of which there were multiple stones.

Attention should be called to the fact that a number of the calculi were soft in consistency, although they contained sufficient calcium to permit their visualization on the roentgenogram. They were indistinguishable, grossly, from the inspissated fecal particles found so commonly in surgically removed appendices. It is possible that some of these soft masses represent true appendiceal calculi.

Chemical Composition Maver and Wells (40) state that the usual composition of appendiceal stones is 1/4, by weight, inorganic material, chiefly calcium phosphates, 1/5 organic residue, mostly vegetable fibers, and 1/2 substances soluble in fat solvents, chiefly soaps, coprosterol, and small amounts of cholesterol. Other authors have reported varying amounts of magnesium ammonium phosphate (64) and

calcium carbonate (7), and absence or faint traces of bile salts and pigments (3), urates (29), silica (61), and iron (64). The stones from Cases 1, 2, and 3 were chemically analyzed and showed an average of 20.3 per cent calcium, 10.3 per cent phosphorus, and 10.8 per cent coprosterol. No magnesium or iron was found, and only traces of cholesterol.

Treatment. Most authors agree that surgery should be performed as soon as the diagnosis is made (32, 59). We feel, too, that the diagnosis of appendiceal calculus is an indication for immediate surgery whether or not the patient has symptoms referable to the appendix. As previously stated, two patients in whom a symptomless calculus was demonstrated by x-ray subsequently had acute appendicitis. If acute symptoms are present, any delay in surgical intervention may have serious consequences because of the danger of perforation. Of 36 cases in which the outcome was mentioned, 4 terminated fatally and 6 had a stormy course but recovered.

SUMMARY AND CONCLUSIONS

From a series of 100 cases reported in the literature and an additional 10 cases reported here, it is concluded that the occurrence of stones in the appendix is a serious and not infrequent condition. The almost constant presence of acute appendicitis in these cases, with an incidence of perforation of nearly 50 per cent, makes the importance of early diagnosis obvious. We have been able to diagnose this condition from roentgenologic evidence in 9 patients. Seven of these were operated upon and the diagnosis was verified.

Once the diagnosis of appendiceal calculus is made, immediate surgery is indicated. The value of roentgenography in acute abdominal conditions is stressed. It is felt that in every case of laminated calcification in the right lower quadrant the diagnosis of appendiceal stone should be entertained and immediate steps be taken to confirm or disprove it.

Sn C, Dr Samuel Rapoport, and Mr A. A. Danish for their assistance in this study.

Cincinnati General Hospital
Cincinnati, Ohio

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SUMARIO

Diagnóstico Roentgenológico de los Cálculos Apéndiceles

De una serie de 100 casos comunicados en la literatura y de otros 10 casos presentados en este trabajo dedúcese que los cálculos del apéndice constituyen un estado grave y no raro. La existencia casi constante de apendicitis en estos casos, con una incidencia de casi 50 por ciento de perforaciones, pone de manifiesto la importancia del diagnóstico temprano. En 9 enfermos de la serie actual se pudo hacer el diagnóstico por los datos roentgenológicos, y 7 de ellos fueron operados, confirmandose así el diagnóstico. Al sospechar litiasis en un caso agudo, los A A acos-

tumbran obtener inmediatamente vistas laterales y anteroposteriores estereoscópicas. Estas películas son estudiadas en húmedo, visto que la perforación, sino ha sobrevenido todavía, debe considerarse como inminente.

Una vez hecho el diagnóstico de cálculo apéndiceles, la intervención cruenta inmediata está indicada. Recálcase el valor de la radiografía en los estados agudos del abdomen. En todo caso de calcificación laminada del hipocondrio derecho hay que considerar el diagnóstico de cálculo apéndiceles.

Bronchiectasis Some Medical Features

Among Military Personnel¹

MAJOR SAMUEL COHEN, M C, A U S

THE ARMY mobilization criteria for induction list bronchiectasis as disqualifying for service. Soldiers with this disease are a definite liability. Screening by chest roentgenography on induction is much more effective in the detection of pulmonary tuberculosis than of bronchiectasis, for the latter may exist in spite of a relatively negative plain roentgenogram. Bronchography is rarely done, if ever, at induction stations. Furthermore, while a careful history alone will frequently suggest a diagnosis of bronchiectasis, this, too, is not a usual part of the examination for entrance into military service.

Next to tuberculosis, bronchiectasis was the most commonly encountered chronic pulmonary infection at the hospital from which this report comes. Altogether 101 cases were definitely diagnosed by lipiodol injection during the four-year period, January 1942 to January 1946. While bronchiectasis among military personnel differs in no respect from the condition in civilians, army life subjects soldiers to physical strains and exposures which usually precipitate hospitalization more promptly for those with pre-existing disease. In this regard, it is worthy of note that in 74 patients, bronchiectasis was diagnosed during a period of hospitalization occurring within the first six months of military service. Also, judging from the past history, 88 of the 101 soldiers had bronchiectasis prior to induction. These figures constitute a definite medical challenge. They are excusable no doubt, in some degree, because of the urgent necessity for the rapid creation of a large army.

The present study afforded an opportunity to review the clinical and roentgen manifestations of bronchiectasis in age groups representing, for the most part,

supposedly healthy individuals. A plea is made for the recognition of the frequency of this disease and its early diagnosis. It cannot be emphasized too strongly that the conventional textbook triad of persistent cough, copious, foul expectoration, and clubbed fingers usually represents far advanced disease. Appropriate therapy, particularly surgical, in suitable cases can be curative. The internist must assume the responsibility for the prompt diagnosis and proper disposition of the bronchiectatic patient.

CLINICAL FEATURES

All but 2 of the 101 patients constituting this series were males, 98 were white and 3 colored. Table I shows the distribution among age groups.

TABLE I AGE DISTRIBUTION OF 101 CASES OF BRONCHIECTASIS

	Cases
Less than 20 years	16
20 to 29 years	56
30 to 39 years	24
40 to 49 years	4
50 to 59 years	1

Past Respiratory History. There is virtual unanimity of opinion that the inception of bronchiectasis can in many instances be traced to childhood. In this series, pulmonary symptoms originated within the first decade of life in 63 cases, during the second decade in 27, and in subsequent years in the few remaining cases. Many soldiers considered their symptoms as trivial. On further inquiry it was found that 83 patients dated their "trouble" from an episode of pneumonia, of whom 49 had one attack and 34 more than one. Thirty-four soldiers also gave a history of pertussis, followed in some instances by pneumonia, in 13 patients measles had

¹ From the Respiratory Diseases Section, Medical Service, Regional Hospital, Fort Bragg, North Carolina. Accepted for publication in October 1946.

been complicated by pneumonia. Pulmonary abscess was apparently the causative agent in one case and aspiration of a foreign body in another. The incidence and role of chronic sinusitis in relation to bronchiectasis could not be adequately evaluated. A history of easy susceptibility to "colds" was common.

Symptoms The pulmonary symptoms were of varying degree. They consisted, in the majority of cases, of a mild to moderate cough, productive of 1/2 to 2 ounces daily of non-foul sputum. Fetid sputum was present intermittently in only 14 patients. The odor is supposedly due to superimposed anaerobic and fusospirochetal infection. While considerable diagnostic emphasis has been placed on this symptom, bronchiectasis should be suspected in many cases despite its absence. In recent years, bronchiectasis has achieved greater recognition as a cause of hemoptysis. The blood is derived from the rupture of submucosal varices in highly vascularized tissue. Hemoptysis was the presenting symptom on admission in 14 patients, and in 18 additional cases the history indicated its occurrence at one time or another. Chest pain, usually mild, inconstant, and non-pleuritic in character, was a complaint in 31 cases, while 40 patients stated that they had some shortness of breath on exertion.

Constitutional symptoms such as fatigability, weakness, anorexia, some loss of weight, and occasional fever, were present in varying degree in 30 cases. Subjective manifestations always have to be carefully evaluated in soldiers. How much a superimposed psychogenic element may have entered into the production of these symptoms would be difficult to state.

Physical Signs The pulmonary signs were not distinctive. That most commonly encountered was persistent râles either alone or in combination with dullness. This was noted in 72 cases. Given a patient with a suggestive history, the existence of the above abnormal findings increases the likelihood of bronchiectasis. Eleven other patients presented dullness

alone, and in 18 no abnormal signs were noted. This, too, is significant. Breath sound changes will depend largely on associated conditions—pleurisy, fibrosis, pneumonitis. Variation in signs before and after postural drainage was noted in some instances. Clubbing of the fingers was present in 13 cases.

ROENTGEN FEATURES

Roentgenography of the chest undoubtedly is of great value, but the use of a radiopaque substance, such as iodized oil, is necessary to establish a definite diagnosis of bronchiectasis. For convenience, the pulmonary roentgen manifestations have been divided into the following groups:

Negative	7 cases
Prominent or "exaggerated"	
pulmonary markings	32 cases
Linear or patchy areas of	
infiltration	44 cases
"Shrunken lobe"	14 cases
Miscellaneous	4 cases

Pleuritic changes, usually of mild degree, were not infrequent. Less noticeable were associated emphysematous areas. Honey-combed shadows of "highlight" were not common. To revert, for emphasis, to the statement of the opening paragraph, it is seen from the above figures that a clear or relatively clear roentgenogram does not in itself preclude bronchiectasis. The clinician should not be led astray in this respect.

Information of interest and value was gained from the induction x-ray films, which were secured and reviewed in 83 cases. Parenchymal infiltration was present in 49, and prominent bronchovascular markings in 19, in 15 cases nothing of special note was seen.

Bronchography is the only method for the positive antemortem diagnosis of bronchiectasis. The character and degree of the ectasia and its pulmonary localization can thus be readily ascertained. Several methods for instillation of lipiodol have been advocated, all give good results, depending upon the skill of the operator carrying out the procedure. There

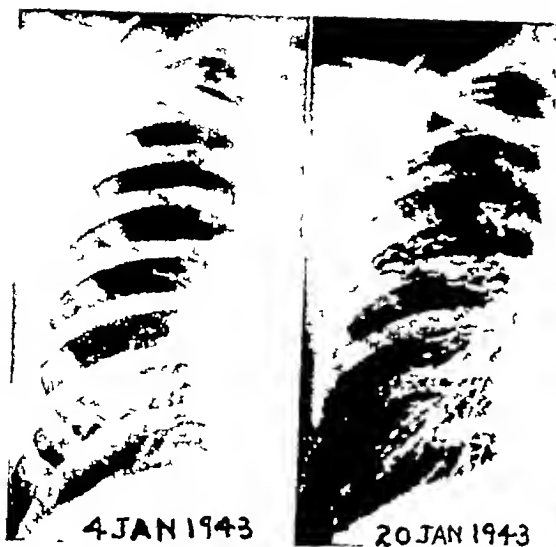


Fig 1 Case 1 Roentgenogram Jan 4 1943, bronchogram, Jan 20 1943

are a few simple but practical and useful hints in bronchography which are worthy of mention (a) Postural drainage before the introduction of the iodized oil is indicated in patients with moderate to copious quantities of sputum. The same procedure should be repeated in all cases immediately after roentgen films have been taken, in order to assure maximum prompt evacuation of the oil from the lungs. The likelihood of a complicating pneumonitis will thus be minimized, and obscuration and faulty interpretation of pulmonary shadows on subsequent films will be lessened. (b) During fluoroscopy, some of the lipiodol may perhaps be seen to have entered the stomach, if so, the prompt administration of a cathartic will eliminate the annoying symptoms of possible iodism. (c) In cases of recent pneumonitis, in which the possibility of underlying bronchiectasis is suspected, bronchography should be deferred until at least two weeks after the complete disappearance of the acute episode, to prevent an exacerbation. (d) A persistent bronchial filling defect with lipiodol is significant and may indicate organic obstruction, with possible bronchiectasis distal to the defect. (e) Prior to consideration of pulmonary resection, adequate visualization with oil of all five lobes is desirable

This is best accomplished in more than one sitting.

In this series, 141 lobes were involved in 101 patients. The left lower lobe was most often affected, 78 times. The diseased area not infrequently was obscured in whole or in part by the cardiac silhouette, and for



Fig 2 Case 2 Roentgenogram, March 28, 1944, bronchogram April 12, 1944

TABLE II ANATOMICAL DISTRIBUTION AND TYPE OF ECTASIA IN 101 CASES (141 LOBES INVOLVED)

	Cases
Unilobar	66
Bilobar	30
Trilobar	5
Left upper lobe	12
Left lower lobe	78
Right upper lobe	5
Right middle lobe	14
Right lower lobe	32
Cylindrical	76
Saccular	20
Mixed	45

that reason lateral or oblique x-ray films are essential. One should not overlook bronchiectasis in the lingula of the left upper lobe. Table II shows the anatomical distribution and the types of bronchiectasis encountered in this series.

Five interesting and illustrative cases have been chosen for presentation.

CASE REPORTS

CASE 1 A 33 year old white male with six years of service was admitted to the chronic chest ward on

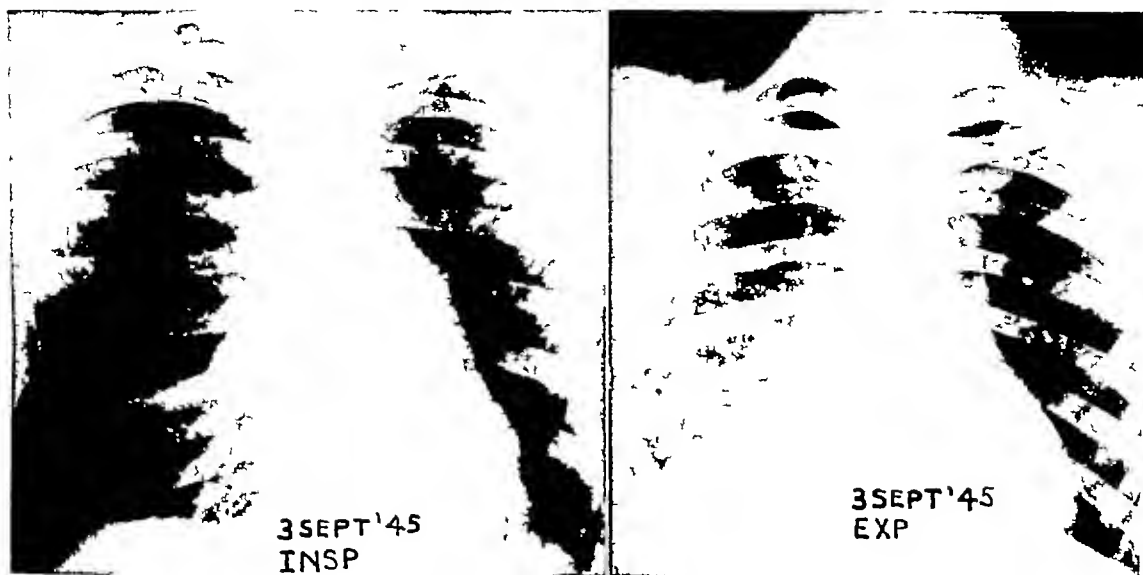


Fig 3 Case 3 Roentgenograms made at end of inspiration and expiration, Sept 3, 1945

Jan 2, 1943, with a history of three attacks of pneumonia since 1934. For the past seven years he had a cough productive of 1/2 to 1 oz of non-foul sputum. He had a small hemoptysis in 1941 and was hospitalized elsewhere, but no definite diagnosis was made. The patient also complained of occasional mild chest pain and slight dyspnea. The right lung showed coarse râles in the second and third anterior interspaces. A roentgenogram on Jan 4, 1943, revealed very slight linear infiltration extending outward from the right hilum where a few small 'honeycombed' areas were seen (Fig 1). Sputum examinations were negative for tubercle bacilli. A bronchogram on Jan 20 (Fig 1) showed definite bronchiectasis in the right upper lobe. The soldier was a valuable man in his organization and was reclassified for limited duty within the continental limits of the United States.

CASE 2 A 19-year old white soldier with five months of military service was hospitalized March 25, 1944. He gave a history of right-sided pneumonia in 1941 with chronic cough since then, yielding about 1 oz daily of non-foul sputum. He was somewhat dyspneic on exertion and had lost 23 lb in weight in two months. The right lung showed dullness and râles over the middle lobe, at the base of the axilla, and posteriorly over the lower lobe. The left lung was clear. Slight clubbing of the fingers was present. An x-ray film of the chest, on March 28 (Fig 2), showed a right sided paracardiac density with linear infiltration along the markings in the lower lung field. The induction film showed similar findings. The bronchogram, April 12 (Fig 2) revealed bronchiectasis of the mixed type involving the lower portion of right upper, right middle and right lower lobe. The line of duty

status was "no," and the soldier was discharged from the army.

CASE 3 A 38-year-old white male with forty-one months of service was admitted Aug 29, 1945, because of abnormal x-ray findings observed at the separation center. The past history was most interesting. In 1911, at the age of four years, while engaged in a fight with his brother, the patient held a safety pin in his mouth, which was aspirated into the chest. Wheezing, cough, and shortness of breath developed and the boy was treated for asthma for several years. The first x-ray examination was made in 1917, when the safety pin was discovered in the left chest. In 1923, while boxing, the patient was struck on the thorax, and the following morning, he coughed up the pin.

This soldier was in an infantry division and had one year of overseas duty. He was evacuated to the United States in March 1944, because, following hospitalization for malaria, the presence of abnormal pulmonary signs and a subsequent roentgen film indicated the possibility of tuberculosis. He was in two general hospitals in this country for nine weeks. Bronchiectasis was diagnosed and he was returned to a limited duty status.

On admission to this hospital the patient appeared well developed and well nourished. Cough and expectoration were very slight. Hemoptysis had never occurred. Dyspnea on moderate exertion was the chief symptom. The chest was emphysematous in contour. The right lung showed hyperresonance. Over the left lung, also, hyperresonance was marked except for an area posteriorly at the base close to the vertebral column where there was dullness with bronchovesicular to bronchial breathing and coarse râles, elsewhere the

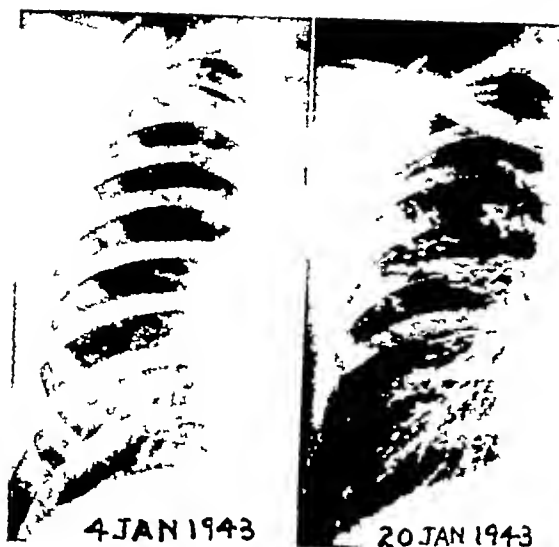


Fig 1 Case 1 Roentgenogram Jan 4 1943, bronchogram Jan 20 1943

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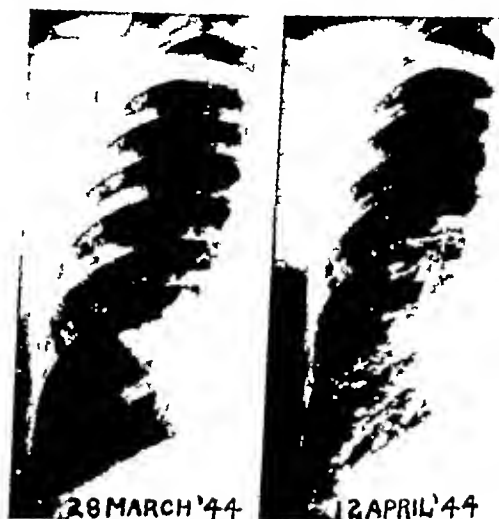


Fig 2 Case 2 Roentgenogram March 28 1944, bronchogram April 12 1944

TABLE 11 ANATOMICAL DISTRIBUTION AND TYPE OF ECTASIA IN 101 CASES (141 LOBES INVOLVED)

	Cases
Unilobar	66
Bilobar	30
Trilobar	5
Left upper lobe	12
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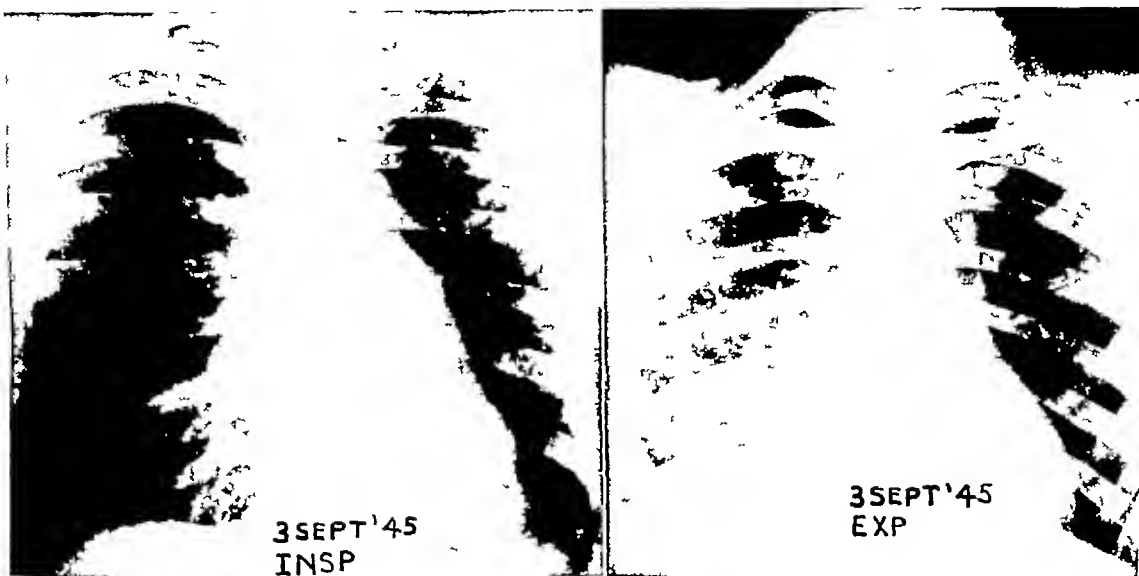


Fig 3 Case 3 Roentgenograms made at end of inspiration and expiration Sept 3, 1945

Jan 2, 1943, with a history of three attacks of pneumonia since 1934. For the past seven years he had a cough productive of 1/2 to 1 oz of non-foul sputum. He had a small hemoptysis in 1941 and was hospitalized elsewhere, but no definite diagnosis was made. The patient also complained of occasional mild chest pain and slight dyspnea. The right lung showed coarse râles in the second and third anterior interspaces. A roentgenogram on Jan 4, 1943, revealed very slight linear infiltration extending outward from the right hilum where a few small "honeycombed" areas were seen (Fig 1). Sputum examinations were negative for tubercle bacilli. A bronchogram on Jan 20 (Fig 1) showed definite bronchiectasis in the right upper lobe. The soldier was a valuable man in his organization and was reclassified for limited duty within the continental limits of the United States.

CASE 2 A 19-year-old white soldier with five months of military service was hospitalized March 25, 1944. He gave a history of right-sided pneumonia in 1941 with chronic cough since then, yielding about 1 oz daily of non-foul sputum. He was somewhat dyspneic on exertion and had lost 23 lb in weight in two months. The right lung showed dullness and râles over the middle lobe, at the base of the axilla, and posteriorly over the lower lobe. The left lung was clear. Slight clubbing of the fingers was present. An x-ray film of the chest, on March 25 (Fig 2), showed a right-sided paracardiac density with linear infiltration along the markings in the lower lung field. The induction film showed similar findings. The bronchogram, April 12 (Fig 2) revealed bronchiectasis of the mixed type involving the lower portion of right upper, right middle and right lower lobe. The line of duty

status was "no," and the soldier was discharged from the army.

CASE 3 A 38-year-old white male with forty-one months of service was admitted Aug 29, 1945, because of abnormal x-ray findings observed at the separation center. The past history was most interesting. In 1911, at the age of four years, while engaged in a fight with his brother, the patient held a safety pin in his mouth, which was aspirated into the chest. Wheezing, cough, and shortness of breath developed and the boy was treated for asthma for several years. The first x-ray examination was made in 1917, when the safety pin was discovered in the left chest. In 1923, while boxing, the patient was struck on the thorax, and the following morning, he coughed up the pin.

This soldier was in an infantry division and had one year of overseas duty. He was evacuated to the United States in March 1944, because, following hospitalization for malaria, the presence of abnormal pulmonary signs and a subsequent roentgen film indicated the possibility of tuberculosis. He was in two general hospitals in this country for nine weeks. Bronchiectasis was diagnosed and he was returned to a limited duty status.

On admission to this hospital the patient appeared well developed and well nourished. Cough and expectoration were very slight. Hemoptysis had never occurred. Dyspnea on moderate exertion was the chief symptom. The chest was emphysematous in contour. The right lung showed hyperresonance. Over the left lung, also, hyperresonance was marked except for an area posteriorly at the base close to the vertebral column where there was dullness with bronchovesicular to bronchial breathing and coarse râles, elsewhere the



Fig 4 Case 3 Bronchogram, Sept 10, 1945

breath sounds were very diminished. There was no clubbing of the fingers. Roentgen films (Fig 3) were obtained at the end of each phase of respiration. It was interesting to note the hyperaeration of the left lung with mediastinal shift and mediastinal pleural herniation to the left after deep inspiration, and the change in the volume and appearance of the right lung with shift of the mediastinum toward the mid line at the end of deep expiration. The bronchogram (Fig 4) showed bronchiectasis in the left lower lobe behind the heart. From a symptomatic point of view, the bronchiectasis was mild. Apparently, the emphysematous changes following aspiration of the foreign body were irreversible and predominant. It is somewhat remarkable that this soldier tolerated his military duties so well in the presence of this pulmonary disability.

The induction x-ray film could not be obtained. The condition undoubtedly antedated entrance into the army, and the patient was discharged via the separation center.

CASE 4 A white private, age 20, was inducted June 21, 1945, and admitted to the hospital Oct 17, 1945, with a history of expectoration of blood that morning. A similar episode had occurred in 1942. The patient had pertussis followed by pneumonia in childhood. Pneumonia (right) was again diagnosed in the winter of 1941. As far back as he could remember, this soldier was subject to frequent attacks of bronchitis productive of scanty non foul sputum. He was well nourished and developed. A few rales

were present at the base of the right lower lobe posteriorly. There was no clubbing of the fingers. A roentgenogram, Oct 18 (Fig 5), showed slight prominence of the bronchovascular markings extending downward from the lower pole of the right hilum. A bronchogram, four days later, revealed definite bronchiectasis beneath the right diaphragmatic shadow. The history in this case was sufficient to point to the proper diagnosis. The line of duty status was "no," and the soldier was discharged.

CASE 5 The patient, a 21-year-old white soldier, entered the hospital with primary atypical pneumonia. Because of slow resolution, with persistence of cough and expectoration, bronchiectasis was suspected and confirmed by bronchography. A careful history elicited no significant respiratory tract infection in the past. There had been two previous army hospitalizations for "sore throat."



Fig 5 Case 4 Roentgenogram, Oct 18, 1945 bronchogram Oct 22 1945, showing definite bronchiectasis beneath the right diaphragmatic shadow

The date of induction was March 22, 1943, and the x-ray film taken at that time was later obtained and interpreted as negative. On Aug 27, 1945, the patient had a sore throat and head cold. The following day he complained of anorexia, malaise, supra-orbital headache, cough, and scanty expectoration. He visited the dispensary and obtained temporary relief. Subsequently, however, the symptoms became aggravated and on admission, Sept 3, 1945, the patient was acutely ill, cyanotic, dyspneic and febrile (103.8°). The leukocyte count was 9,300, with 68 per cent polymorphonuclear leukocytes. A chest x-ray film (Fig 6) taken the same day revealed diffuse bilateral infiltration, more extensive on the right. The patient received oxygen for five days. Because he was desperately sick, penicillin was given empirically (120,000 units daily) for six days without any significant effect. The condition improved gradually and the patient became afebrile in about five weeks. Roentgen resolution was very slow, as

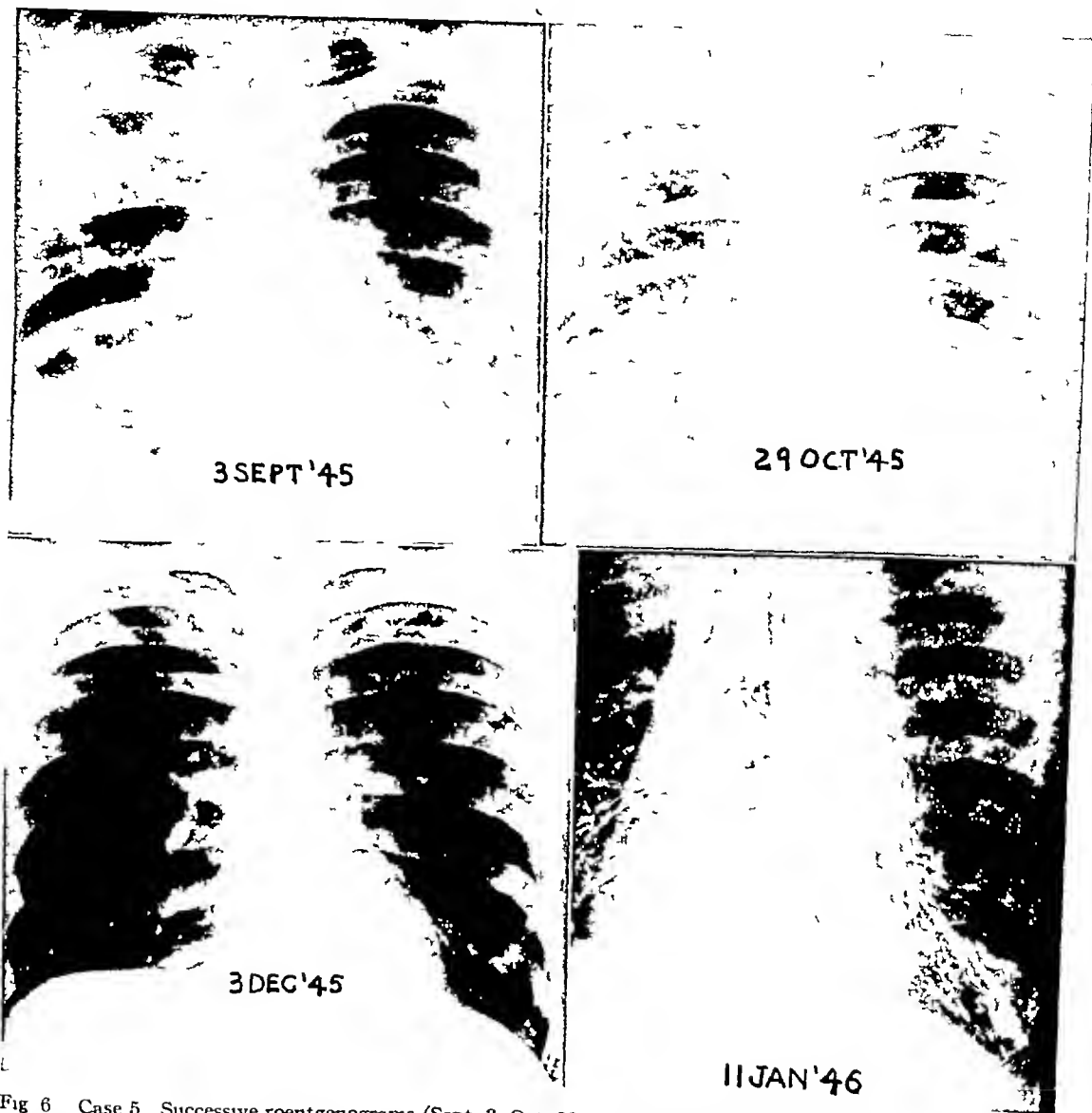


Fig 6 Case 5 Successive roentgenograms (Sept 3, Oct 29 Dec 3 1945) of a patient with primary atypical pneumonia and subsequent development of bronchiectasis as shown by bronchography (Jan 11 1946)

observed on the film of Oct. 29 (Fig 6) By Dec 3, 1945 (Fig 6) further clearing had occurred, with some residual basal linear infiltration, more evident on the left Cough continued, with about 1 oz of non foul sputum daily A liberal time interval was allowed to elapse before injection of lipiodol, to avoid a recurring pneumonitis Finally, on Jan 11, 1946, a bronchogram (Fig 6) showed bronchiectasis in the posterolateral segment of the left lower lobe Whether the affected lobe was permanently damaged cannot be stated as this patient was transferred to a thoracic disease center nine days later

DISCUSSION

The diagnosis of bronchiectasis and the prompt and proper disposition of the af-

fected soldiers was the main medical obligation with respect to this disease at this hospital For various reasons, bronchoscopy was not a routine procedure Ideally, every patient with bronchiectasis should have at least one such examination Unquestionably, significant intrinsic changes and an unsuspected foreign body may sometimes be discovered Pending disposition, therapy consisted of symptomatic medication and postural drainage in those with moderate or excessive expectoration A few patients received chemo-

therapy, sulfadiazine orally or penicillin parenterally, but the period of observation was too short to permit a definite conclusion as to its value.

The line of duty status was "yes" in 13 cases and the patients were transferred to general hospitals (thoracic disease centers) for further evaluation, according to army directives. For 88 patients the line of duty status was "no" 10 were returned to limited duty and 78 were separated from the service. These soldiers were instructed about their disease and strongly advised to have close medical attention on return to civil life. The curative effect of lobectomy in the hands of competent thoracic surgeons was emphasized to suitable patients.

In all fairness it should be mentioned that a number of patients were seen with a history of bronchopulmonary symptoms, frequently in association with abnormal physical and roentgen findings, in whom a presumptive diagnosis of bronchiectasis seemed justifiable but actual dilatation of bronchi could not be demonstrated by bronchography. These cases probably represent instances of bronchitis with or without some degree of pulmonary fibrosis. It is inevitable that there will be a percentage of normal bronchograms in any such clinical survey. At the same time there were encountered cases of doubtful bronchiectasis exhibiting slight variations of the so-called normal bronchial tree. As in other medical observations, the line of cleavage between normal and abnormal is sometimes imperceptible and subsequent re-examinations alone can make the final decision. In this connection, reference should be made to what Blades and Dugan (1) have described as "pseudo-bronchiectasis"—slight temporary bronchial dilatation which may follow primary atypical pneumonia and last for one to three months, with eventual reversion to normal. Such a term, however, is confusing, "reversible bronchiectasis," as used by Fleischer (2) is more logical.

Pneumonia, especially of the bacterial, lobular, and slowly resolving type, has

long been recognized as an important etiologic agent in bronchiectasis. More recently, particularly during the war, primary atypical or "virus" pneumonia has attracted increasing attention, and the question of bronchiectasis as a complication in such cases deserves consideration. In what is probably the best article to date on the pathologic anatomy of atypical pneumonia, Golden (3) analyzed the changes in 42 autopsied cases. To quote

"The acute dilatation of affected bronchioles is observed fairly constantly. One would expect that complications might ensue, such as chronic bronchiectasis. To date no case in which this occurred has come to my attention pathologically. On the other hand, actual necrosis of bronchial walls was seen but once. In the remainder of the cases the lesions were of two types. In lesions of one type the bronchial walls were merely edematous, congested and heavily infiltrated with round cells. It is perfectly consistent with the known processes of repair that such lesions could resolve without leaving any appreciable damage. In lesions of the other type, frequently seen in the same case, one could demonstrate in small bronchi and bronchioles marked dilatation, destruction of the elastic fibers, fragmentation of the muscle bundles and shredding of the reticular meshwork. Such lesions probably could heal only by persistent dilatation and scar formation. This is not meant to imply that all such lesions could or would ever become clinically manifest as chronic bronchiectasis."

Kay (4) reported 20 cases of bronchiectasis (3 with reversible and 17 with permanent damage) following attacks of atypical pneumonia. Apparently none of his series had pulmonary symptoms prior to the pneumonia. The incidence of bronchiectasis was not known.

It may appear superfluous to mention that in this connection one should be certain that the patient was first afflicted with atypical pneumonia. There is no doubt that in the past few years this disease has been over-diagnosed in many army installations. The difficulty of differentiating borderline cases of atypical pneumonia from bacterial pneumonia and influenza is only too often apparent and the problem is further aggravated by the fact that secondary bacterial invasion may probably, in some instances, be superimposed on the virus infection. It should also be recalled

that acute inflammatory exacerbations may occur in association with pre-existing bronchiectasis and chronic interstitial pneumonitis

At this hospital, bronchograms were done on patients with atypical pneumonia who had very slowly resolving or recurrent episodes with persistence of abnormal physical and/or roentgen signs. In only 9 cases was there definite evidence of bronchiectasis. Unfortunately this cannot be expressed on a statistical basis. Some of the remainder may represent, as Kay has suggested, intermediate changes in the development of bronchiectasis, but only a prolonged follow-up could furnish the correct answer. The problem is of interest and importance, and further study in this direction is necessary. One thing is certain. To minimize bronchiectasis as a complication, the ideal solution is to refrain from returning soldiers to duty until maximum clearing has occurred on physical and x-ray examination.

SUMMARY AND CONCLUSIONS

1 One hundred and one patients with bronchiectasis, diagnosed by bronchography, were admitted during a four-year period (1942-1945, inclusive) to a large army hospital. The pertinent clinical and roentgen features are reviewed.

2 The chief function at this hospital with respect to this condition was the diagnosis and proper disposition of the bronchiectatic patient. Eighty-eight soldiers had the disease prior to induction, 78 were discharged from the service and 10 were

returned to limited military duty. Thirteen soldiers who contracted the disease in line of duty were transferred, according to army directives, to appropriate general hospitals for further study.

3 Bronchiectasis is a common disease. A plea is made for its early recognition. It may exist in the absence of classical symptoms and signs. The screening process on induction is not always conclusive. Furthermore, 39 of the hospitalized soldiers had negative or relatively negative plain roentgenograms. A careful history and a healthy suspicion of bronchiectasis will frequently lead to the diagnosis, but—

4 Bronchography is the only certain method of confirming the diagnosis. Several useful points in bronchography are mentioned. The anatomical distribution and the type of bronchial ectasia encountered in this series are tabulated. The left lower lobe was most commonly involved and cylindrical dilatation was most often noted.

5 The role of primary atypical pneumonia in the development of bronchiectasis is discussed.

B. S. Pollack, Hospital for Chest Diseases
100 Clifton Place
Jersey City 4, N. J.

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SUMARIO

Bronquiectasia en el Personal Militar

Durante un cuatrienio (1942-1945) ingresaron en uno de los más grandes hospitales militares de los E. U. A. 101 enfermos con bronquiectasia diagnosticada por la broncografía. Ochenta y ocho padecían de la enfermedad desde antes de su ingreso en el ejército. 78 fueron dados de baja del servicio militar y 10 fueron reintegrados

en las filas. Trece que contrajeron la afección mientras servían en el ejército fueron trasladados para estudio ulterior a hospitales generales apropiados.

La bronquiectasia es una enfermedad frecuente, y aquí se aboga en pro de su reconocimiento temprano. Puede existir aun faltando los síntomas y signos clásicos.

therapy, sulfadiazine orally or penicillin parenterally, but the period of observation was too short to permit a definite conclusion as to its value.

The line of duty status was "yes" in 13 cases and the patients were transferred to general hospitals (thoracic disease centers) for further evaluation, according to army directives. For 88 patients the line of duty status was "no" 10 were returned to limited duty and 78 were separated from the service. These soldiers were instructed about their disease and strongly advised to have close medical attention on return to civil life. The curative effect of lobectomy in the hands of competent thoracic surgeons was emphasized to suitable patients.

In all fairness it should be mentioned that a number of patients were seen with a history of bronchopulmonary symptoms, frequently in association with abnormal physical and roentgen findings, in whom a presumptive diagnosis of bronchiectasis seemed justifiable but actual dilatation of bronchi could not be demonstrated by bronchography. These cases probably represent instances of bronchitis with or without some degree of pulmonary fibrosis. It is inevitable that there will be a percentage of normal bronchograms in any such clinical survey. At the same time there were encountered cases of doubtful bronchiectasis exhibiting slight variations of the so-called normal bronchial tree. As in other medical observations, the line of cleavage between normal and abnormal is sometimes imperceptible and subsequent re-examinations alone can make the final decision. In this connection, reference should be made to what Blades and Dugan (1) have described as "pseudo-bronchiectasis"—slight temporary bronchial dilatation which may follow primary atypical pneumonia and last for one to three months, with eventual reversion to normal. Such a term, however, is confusing, "reversible bronchiectasis," as used by Fleischner (2) is more logical.

Pneumonia, especially of the bacterial, lobular, and slowly resolving type, has

long been recognized as an important etiologic agent in bronchiectasis. More recently, particularly during the war, primary atypical or "virus" pneumonia has attracted increasing attention, and the question of bronchiectasis as a complication in such cases deserves consideration. In what is probably the best article to date on the pathologic anatomy of atypical pneumonia, Golden (3) analyzed the changes in 42 autopsied cases. To quote

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Uptake of Radioactive Iodine by the Normal and Disordered Thyroid Gland in Children

A Preliminary Report

EDITH H. QUITMBY, Sc D., and DONOVAN J. McCUNE, M.D.

Columbia University, New York, N. Y.¹

STUDIES OF THE uptake of radioactive iodine by the normal and hyperfunctioning thyroid gland in adults have been published by Hamilton and Soley, Hertz, Roberts and Salter, (1, 2) and others. Hamilton, Soley, Reilly, and Eichorn have reported on iodine studies in a small series of cases of childhood hypothyroidism, including some with goiter (3). Most of their tests were made with eight-day iodine containing an appreciable admixture of stable iodine, with such material the apparent uptake is always much less than with a "carrier-free" preparation in which all the iodine is radioactive.

Since the search for an unambiguous indicator of thyroid function in children, particularly in infants, still continues, the present study was undertaken in the hope of achieving this goal.

Eight-day radioactive iodine (I^{131}), carrier-free, was obtained from the cyclotron laboratory of the Massachusetts Institute of Technology in dilute solution of sodium iodide. The amount of the latter was so small as to be considered physiologically negligible. The material was administered quantitatively by mouth, a stomach tube being used in the case of infants and uncooperative small children. The subjects were not fasted. The doses varied from 20 to 40 microcuries (containing not more than 2 micrograms of iodine) in about 20 cc of solution. Smaller amounts were given to babies than to older children, but they were not calculated accurately on a weight basis.

The relative quantities of the iodine concentrated in the thyroid glands were de-

termined by measurements with a shielded Geiger counter placed in a fixed position over the front of the neck. These were related to the administered doses by measurements in the laboratory with a "phantom" set-up approximating the geometrical relationships with the patient. Whenever possible, all urine was collected for two successive 24-hour periods for measurement of the amount of iodine excreted.

Pathological cases were selected chiefly on the basis of medical interest; this resulted in the study of infants and children of from three weeks to fourteen years. To eliminate differences in uptake due to possible variations in the material received from the cyclotron, an effort was made to study a control child of the same age and of approximately the same size simultaneously with each patient. The controls all came from the hospital population. While none showed features which justified the suspicion of "glandular" disorder, no matter how vague, only a few were strictly well children. The majority were suffering from, or in convalescence after, various illnesses, such as infection, diarrhea, or nutritional disorder, which can certainly be conceived to have affected temporarily the state of activity of the thyroid gland. The precaution of studying a control at the same time as the patient proved unnecessary, since significant variations in the quality of the test material were not detected.

Fifty-four subjects are included in this report, two or three tests were done on a few. Twelve were infants under one year. Of these, 11 were controls, the other had

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Además, 39 de los soldados hospitalizados mostraron radiografías simples negativas o relativamente negativas. Un interrogatorio cuidadoso y una sospecha justificada de la existencia de bronquiectasia conducirán frecuentemente al diagnóstico acertado, pero la broncografía constituye el único método seguro para confirmarlo. La naturaleza e intensidad de la ectasia y su

localización pulmonar pueden averiguarse fácilmente en esa forma. En la serie actual el lóbulo inferior del pulmón izquierdo representó el asiento más frecuente y la dilatación cilíndrica la forma predominante.

Discútese el papel desempeñado por la neumonía primaria atípica en la producción de la bronquiectasia pero sin llegar a conclusiones estadísticas.



TABLE II URINARY EXCRETION OF RADIOACTIVE IODINE IN CONTROLS
(Per Cent of Oral Dose)

Case	0-8 Hours	8-16 Hours	16-24 Hours	24-48 Hours	Total
L R	44	28	4	3	79
A P	33	19	13	4	69
R E	25	25	8	9	77
M C	7	21	10	7	Incomplete
R P	13	35	5	13	66
D D	25	9	No specimen	12	Probably incomplete
E S	Two days' specimens assembled				68
A R	44	8	Incomplete	0	Incomplete
J P	49	0	11	2	62
C P	Lost	25	11	19	Incomplete

TABLE III PER CENT OF RADIOACTIVE IODINE IN THYROID GLANDS OF ABNORMAL SUBJECTS

Case	Diagnosis	Age	Per Cent Uptake, 48 hr	Per Cent Excretion, 48 hr
Known Thyroid Disorder				
S B	Sporadic cretinism	2 mo	Less than 1	
E M	Sporadic cretinism	16 mo	Less than 1	
T A	Sporadic cretinism	2 yr	Less than 1	
L B	Sporadic cretinism	14 yr	Less than 1	
J A	Surgical myxedema	12 yr	Less than 1	70
J R	Graves' disease	9 yr	60	Less than 10
J M	Graves' disease	10 yr	34	
Y S *	Slightly enlarged thyroid	14 yr	20	49
	Probably diffuse colloid goiter			
C P	Colloid adenoma of thyroid	12 yr	3	
	No evidence of hypothyroidism			
	Repeated test		3	71
Other Abnormals				
A P	Dwarfism	7 mo	6	
L G	Dwarfism, extremely questionable hypothyroidism non-responsive to treatment	2 yr	8	
J F	Dwarfism	2 yr	6	
D K	Dwarfism, questionable hypothyroidism	7 yr	5	
A N	Dwarfism	8 yr	21	54
M N	Dwarfism nutritional difficulty	9 yr	17	44
P F	Dwarfism	12 yr	0 5	87
D O	Progeria (?)	16 mo	30	
	After 2 months on thiouracil		11	
	Four months after stopping thiouracil		21	
D T	Gargoylism	2 yr	9	
L B	Slight sexual precocity	3 yr	21	
	Adrenal-cortical tumor (?)			
S H	Hypoparathyroidism (idiopathic)	10 yr	6	
	No evidence of hypothyroidism			
D B	Pheochromocytoma of adrenal	12 yr	13	64

* This patient had been on iodine therapy for six months, it had not been discontinued prior to the test. Her basal metabolic rate, cholesterol, and blood iodine were all normal. She was suspected of hyperthyroidism but could not be expected to show an elevated radio iodine uptake under these circumstances.

With the exception of the patient mentioned in the previous paragraph, only patients with clear-cut hypothyroidism had values so low. However, quite low concentrations were observed not only in those individuals who presented unequivocal evidence of hypothyroidism but also in some who failed entirely to suggest this

possibility. Attention may be drawn to P F, a white boy of twelve years whose stature was about that of a six-year-old. The history, physical features, and laboratory evidence pointed to non-endocrine dwarfism or, at most, to dwarfism due to unique deficiency of the growth-promoting secretion of the hypophysis. The low re-

TABLE I PER CENT OF RADIOACTIVE IODINE IN THYROID GLAND IN CONTROLS AT 48 HOURS AFTER ORAL ADMINISTRATION

Infants to 1 year		Children 1-4 years		Children 5-14 years	
Name	Per Cent	Name	Per Cent	Name	Per Cent
T P	10	E G	10	M B (adult)	10
M F	7	P M	4	L A	15
P C	15	D A	7	B B	9
J L	15	R H	11	L R	18
W T	10	J G	12	A P	15
J B	11	G M	15	H G	13
V P	9	E S	10	R C	12
H V	12			J P	20
P T	9	Average	9.9	M M	15
M T	20	$\sigma =$	3.3	S T	13
E G	17			M C	11
				A R	12
				R P	17
Average	12.3			E S	12
$\sigma =$	3.7			D D	12
				Average	13.5
				$\sigma =$	2.9
				Total mean	12.0
				$\sigma =$	3.6

been recognized as a cretin at the age of three weeks. Fifteen were between one and four years of age, 7 were controls as defined above, 2 were classical cretins, 1 showed some features of hypothyroidism which were not modified by treatment, 2 were dwarfs, in 1 the diagnosis was "gargoylism", 1 was suspected of progeria, a disorder associated with some of the features of hypothyroidism, and the last exhibited features of moderate sexual precocity. Twenty-seven were more than four but less than fifteen years of age. Of these 2 had unmistakable hypothyroidism, 2 Graves' disease, 1 questionable hyperthyroidism. Four were dwarfs, of these, 1 showed debatable signs of reduced thyroid function. One had a colloid goiter of small dimensions and showed no evidence of alteration of thyroid function. One had an adrenal pheochromocytoma, and 1 idiopathic hypoparathyroidism without evidence of hypothyroidism. Fifteen served as controls—again in the sense already defined.

Measurements on a few children were started shortly after administration of the material and carried out at intervals through the day for several days thereafter. Others were measured only daily for a few

days and then at longer intervals. It was found that the values are substantially constant from the first through the fourth day, when correction is made for radioactive decay. Therefore, for convenience of comparison, the 48-hour reading was arbitrarily selected. These 48-hour readings for the controls are given in Table I, with averages and standard deviations.

Measurements of excretion were possible in only the five- to fourteen-year group and not in all of these. Some specimens were frequently lost. The available data for controls are given in Table II. It appears that excretion is rapid and that the totals are fairly constant but would not be satisfactory as an index of uptake.

Table III presents the data relating to the concentration of iodine in the neck region of the hypothyroid and hyperthyroid individuals and of those who had, or for one reason or another may be considered suspect of, some endocrine disorder.

The few observations that were made on the excretion of iodine in the urine of these individuals appear in Table IV.

DISCUSSION

In view of the preliminary character of this communication and the limited nature of the data, it does not appear warranted to discuss them in great detail.

As regards the controls, the mean value for uptake is 12.0 per cent with a standard deviation of 3.6.

One feature stands out in the group of abnormal subjects, namely, the extremely small retention in the case of the individuals with indisputable hypothyroidism. J. A. suffered from complete athyreosis occasioned by the inadvertent removal of a small, spherical mid-line undescended thyroid gland which was erroneously taken to be a thyroglossal duct cyst. Her uptake was essentially zero. The cretins, although their defect of glandular substance appeared to be complete on clinical grounds, concentrated enough iodine to suggest that traces of the gland were present, thus confirming a common anatomic observation in cretinism.

SUMARIO

Absorción de Yodo Radioactivo por el Tiroides de los Niños

La administración a los niños, incluso lactantes, de yodo radioactivo, sin portador, por vía bucal, a dosis de 20 a 40 millicuries va seguida de concentración y retención en el tiroides de cantidades que varían de aproximadamente 12 por ciento en personas sin distiroidia manifiesta a varias veces dicha cifra en el hipertiroidismo y menos de 1 por ciento en los hipotiroideos típicos. Encuéntrense cifras considerablemente inferiores al promedio, y de cuando en cuando tan bajas como las del hipotiroidismo indudable, no sólo en individuos dudosamente hipotiroideos sino

también en algunos cuya función tiroidea queda más allá de toda sospecha clínica de insuficiencia. Estas limitaciones de la interpretación dependen sin duda en parte de que tanto el hipertiroidismo como el hipotiroidismo son estados relativos de intensidad variable. Sin embargo, el estudio no numérico de los datos disponibles indica que cabría obtener resultados más netos mediante una estandarización más cuidadosa de la prueba con respecto, entre otras cosas, a la previa ingestión de yodo por el enfermo y el estado de su salud en la fecha de la observación.

(For discussion of this paper, see page 229)



TABLE IV
EXCRETION OF RADIOACTIVE IODINE IN THE URINE OF ABNORMAL SUBJECTS
(Per Cent of Dose)

Name	0-8 Hours	8-16 Hours	16-24 Hours	2d Day	3d Day	Total
J A	First 24 hours		32	32	6	70
Y S	First 24 hours		30	19		49
J R	8	Less than 1	Less than 1	Less than 1		Less than 10
P F	50	3	20	14		87
A N	30	4	14	6		54
C P	Lost	25	11	12		Incomplete
Repeat	35	15	10	5		71
D B	9	16	11	8		64
M N			39	5		44

tention and rapid excretion of iodine can certainly not be ascribed to hypothyroidism of any recognizable variety or degree. Since the boy came from a part of the country where iodized table salt is commonly used, saturation of the gland is a possible explanation, but the history failed to reveal information on this point. His basal metabolic rate, calculated by three standards, was +60. However, this is doubtless wrong. It should be pointed out that there are no satisfactory standards for dwarfs. C. P. had a small colloid adenoma of her gland but was normal in all other respects. The idiopathic or cryptogenic hypoparathyroidism which S. H. exhibited was not accompanied by any signs whatever of reduced function of the thyroid gland.

A second but somewhat less impressive feature in the group of abnormal subjects is the high value in the two cases of Graves' disease and the elevated retention in the single case of what is probably progeria.

As was stated in the introduction, the excretion of iodine in the urine was confirmatory of the uptake by the gland. Discrepant results should serve to call attention to the possibility of technical error in one or the other of the measurements or to the loss of specimens of urine. Since in young children the need to collect urine quantitatively over a considerable period of time imposes a serious restriction on the feasibility of any test, this part of the study has not been pursued with great zeal.

CONCLUSIONS

The administration to infants and children, by the oral route, of carrier-free radio-

active iodine in doses of from 20 to 40 microcuries is followed by concentration and retention within the thyroid gland of amounts which vary from about 12 per cent in those without evident thyroid disorder, upward to severalfold this value in hyperthyroidism and downward to less than 1 per cent in those who are typically hypothyroid. Values considerably below the mean, and occasionally as low as those in unmistakable hypothyroidism, are found not only in individuals who are only dubiously hypothyroid but also in some whose thyroid function is quite beyond clinical suspicion of insufficiency. These limitations to interpretation doubtless depend in part on the fact that hyperthyroidism and hypothyroidism are both relative states and show variability of degree. However, non-numerical examination of the data suggests that sharper results could be obtained by more careful standardization of the test with respect, among other things, to the patient's previous intake of iodine and the state of his health at the time of the observation.

630 W. 168th St.
New York 32, N. Y.

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during the preliminary studies in which the method was developed (6)

MATERIAL AND METHODS

After the thyroid tissue containing the radioiodine has been preserved, dehydrated, and embedded according to usual histologic procedures, the paraffin sections are cut at $10\ \mu$ or less. The ribbon is separated into groups, containing two or more sections. These are then placed on the surface of water in a Petri dish at the proper temperature to produce spreading of the sections (approx 42°C). After the sections have expanded, the Petri dish is taken into the photographic darkroom and dropped gently into a larger bowl of cool water, allowing the ribbons to float free. Then, in the dark and in front of a dim red safe-light, the red insensitive film or plate is slipped under a strip of tissue sections. The strip is held against the emulsion with a needle or small brush, and the plate plus the tissue is removed from the water. The preparation is dried and stored upright in a light-tight box. The following day the plates are immersed in xylol until the paraffin has been removed. The plates are then returned to the storage container until the radiation exposure has been completed. The proper exposure time is determined by trial and by amount of activity as indicated by the Geiger counter. When the exposure to the radiation has been completed, the photographic plate with the tissue section still in place is developed, fixed, and washed, and is allowed to dry before further processing. The tissue is then stained with Harris' hematoxylin (over stain-wash-acid water-wash-alkaline water-wash) and counterstained with eosin. The preparation is dehydrated in alcohols, cleared in xylol, and mounted in clarite, or balsam.

Lantern slide plates, Eastman median contrast, are satisfactory for the autographs. The 2×2 -inch size is convenient for the tissue-autograph preparation and the $3\frac{1}{4} \times 4\frac{1}{4}$ -inch size is used for the older method in which the microscope slide containing the tissue is taped to the photo-

graphic plate during the radiation exposure. It is best to produce both types of autographs as a check on proper development and penetration of solutions, etc. The lantern slide plates are reasonably radiosensitive, the grain is fairly uniform, and it is possible to stain the tissue section on the plate without making the color of the emulsion too heavy. The tissue-photographic plate preparation should be dried as often as possible, solutions should not be warm, and strong acids are to be avoided.

Dental x-ray film (Eastman ultra-speed safety film) is more sensitive to the radiation, but the final preparation is not as clear as when lantern slides are used. The film is used when quick results are desired. Recently, sections of a thyroid adenoma containing radioiodine produced satisfactory autographs with a radiation exposure of only sixteen hours. An hour later the preparations had been stained, mounted in glycerine jelly, and were being studied under the microscope. Permanent preparations may be made with film, but the staining of the film is heavy and it tends to curl in the xylol. Coloring of the film may be avoided to some extent by staining the tissue *in toto* (acetocarmine or alcoholic eosin) as it is being preserved. Care must be exercised, however, not to wash out the stain completely in subsequent treatment, and a counter stain must be added after the tissue has been mounted on the film. If the film is dried in air, after the tissue has been stained, then rapidly put through the alcohols and xylol, the tendency to curl will not be great. The film may then be trimmed, mounted in balsam, and held flat while drying by means of a small weight on the cover slip. The tissue may also be stained with Harris' hematoxylin (either before dehydrating, or later as the sections are spreading in the warm water) before it is placed on the film, but again most of the stain is lost in subsequent treatment. A mordant, ferric alum, may be added to the preservative (7) so that later, when the tissue-autograph preparation is immersed in iron hematoxylin, the

Preparation of Radioautographs of Thyroid Tumors for Study at High Magnification¹

TITUS C EVANS, Ph D

Radiological Research Laboratory, Department of Radiology, Columbia University, New York, N Y

ONE OF THE methods of studying iodine uptake of thyroid tumors is to make radioautographs of thin sections of the tissue. The usual procedure (1-4) is to place the tissue section, mounted on a microscope slide, against a photographic emulsion for a suitable time in the dark. After the radiation exposure, the two plates are separated. The photographic image is developed, the tissue section is prepared for histologic examination, and the two are compared. In most instances the autographs give clear evidence as to whether the tissue has accumulated radioiodine and, if so, in what general region. The plate containing the autograph may be superimposed on the tissue preparation to permit further localization of the radioiodine. With this method, the exact location of the radioiodine is difficult to determine, as at higher magnifications the alignment of the two preparations becomes arbitrary and the outlines of the denser areas of the autograph are not distinct.

It is apparent that closer contact between the tissue and the photographic plate is to be desired, also, that a more objective alignment of the tissue and autograph would be obtained if the two did not have to be separated after the radiation exposure had been made. It occurred to us that, as one of the standard procedures in microtechnic is to float paraffin sections onto the microscope slide, it would be worth while to try such a method of mounting tissue directly on a photographic plate. It seemed probable that the tissue would adhere to the photographic emulsion and would permit passage of the photographic chemicals as well as those used in the histologic technic. At the time that preparations for this experiment were under way, a method of attacking this

problem was published by Bélanger and Leblond (5). This consists of removing the emulsion from an unexposed lantern slide and spreading it over the tissue section. After proper exposure to the radioactive material contained in the tissue, the emulsion is developed and fixed. The preparation is then subjected to the usual histologic staining procedures. This method permits close contact between the tissue and the photographic plate. Also, the histologic preparation and the autograph are automatically superimposed.

This method seemed to offer a solution of the problems outlined above, so it was tried along with the usual technic. The results were better than with the older method, but several objectionable features developed. The transposed emulsion varied in thickness, developed a heavy "fog," softened easily, and tended to lift away from the tissue section. The emulsion became heavily stained, and study at high magnification was difficult. No doubt some of the faults were due to inexperience and could have been eliminated in time. It seemed advisable, however, to try mounting the tissue directly on a photographic plate. This method has been found to be satisfactory, and results are much better than those previously obtained.

Sections of thyroid adenoma, etc., containing radioiodine produce good tissue autographs as the follicles are usually surrounded by stroma so that the localization is more distinct than when several follicles are close together and their radiation fields overlap. This report will be limited to a demonstration of results attainable with radioiodine in human thyroid tumors, but the method is applicable to other radioactive substances and other tissues as well. The thyroid region of the rat was employed

¹ Accepted for publication in March 1947



Plate II A Photomicrograph ($\times c 520$) of thyroid adenoma section mounted on photographic plate. The individual grains of reduced silver in the emulsion may be seen. Enough of the photographic image was in the same plane of focus as the tissue to permit this single picture showing the heaviest concentration of radioiodine to be within the follicle.

B Photomicrograph ($\times c 620$) of section of another thyroid adenoma mounted directly on photographic emulsion. The plane of focus is slightly below that of the cells and the heavy accumulation of reduced silver grains may be seen in the region of the colloid.

tissue is selectively stained. Caution must be used if ferric alum is employed to differentiate after hematoxylin, as it acts to reduce the photographic image to some extent.

If it is desired to reduce the photographic image, the plate may be immersed in iron alum or a weak solution of permanganate (8) until the desired contrast has been reached.

RESULTS

Two surgical specimens of thyroid adenoma were provided through the courtesy of Dr V. Kneeland Frantz, Department of Surgical Pathology. These patients had been given 1 me of I^{131} twenty-four hours before removal of the glands. Material was removed from these adenomas, and regions indicating the presence of radioiodine (detected by Geiger counter) were preserved in Boun's solution, dehydrated, and embedded in paraffin. Sections were

cut at 10μ . An autograph made in the usual way, *i.e.*, slide bearing tissue separate from photographic plate, is shown in Fig A of Plate I. The corresponding tissue section is shown in Fig B of this plate. It is easy to determine the general location of the radioiodine with an autograph as distinctive in pattern as this one. It may be determined by inspection and by measurement that the radioiodine is chiefly at the base of the triangular section and in the lower part of the upper section. Further localization is difficult, as at high power a certain region of the autograph appears very diffuse (Fig D, Plate I). It is not easy to match Fig D with Fig E to determine the exact location of the radioiodine. The tissue-autograph preparation at low magnification ($\times 215$) is shown in Fig C of Plate I. Although this specimen is many sections removed from that of Fig B, it is from the same region of the tumor,

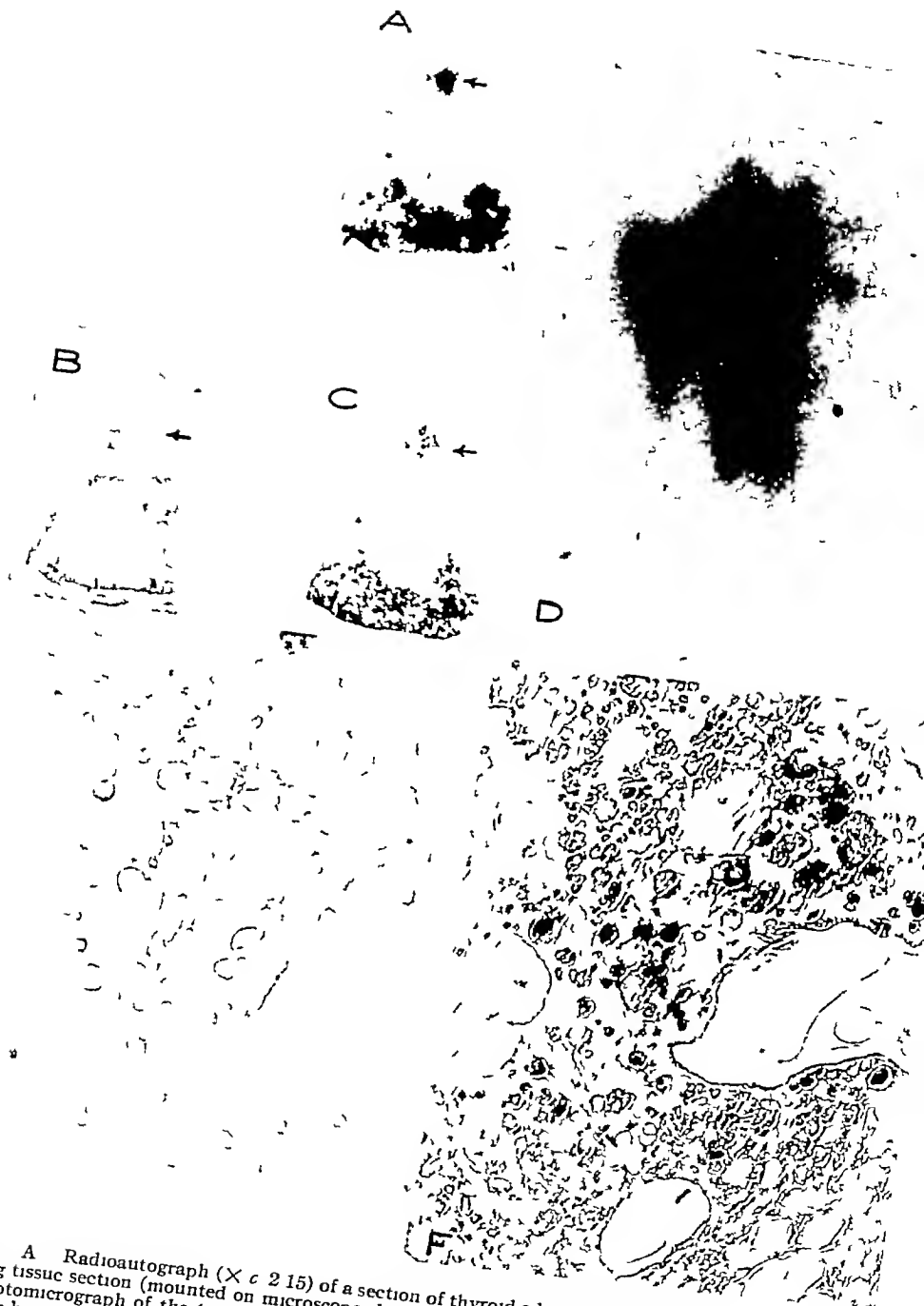


Plate I A Radioautograph ($\times c 215$) of a section of thyroid adenoma containing radioiodine Made by placing tissue section (mounted on microscope slide) against a photographic plate
 B Photomicrograph of the tissue section used in making the above radioautograph ($\times c 215$) The section has been inverted so as to give orientation similar to that of A
 C Photomicrograph ($\times c 215$) of tissue autograph preparation inverted to correspond in position with A and B of a section from the same block of tissue used for A
 D Photomicrograph of a portion of the autograph image marked with arrow in 4 at higher magnification ($\times c 33$)
 E Region of B marked with arrow $\times c 33$ The relative positions of left and right sides have been reversed as compared to above figures
 F Tissue autograph preparation oriented similarly to E and at the same magnification One should not attempt to identify details of Fig F in Fig E as they are many sections apart although from the same general region The follicles containing the radioiodine are indicated by darkened areas of the photographic emulsion, which is in place directly under the tissue.

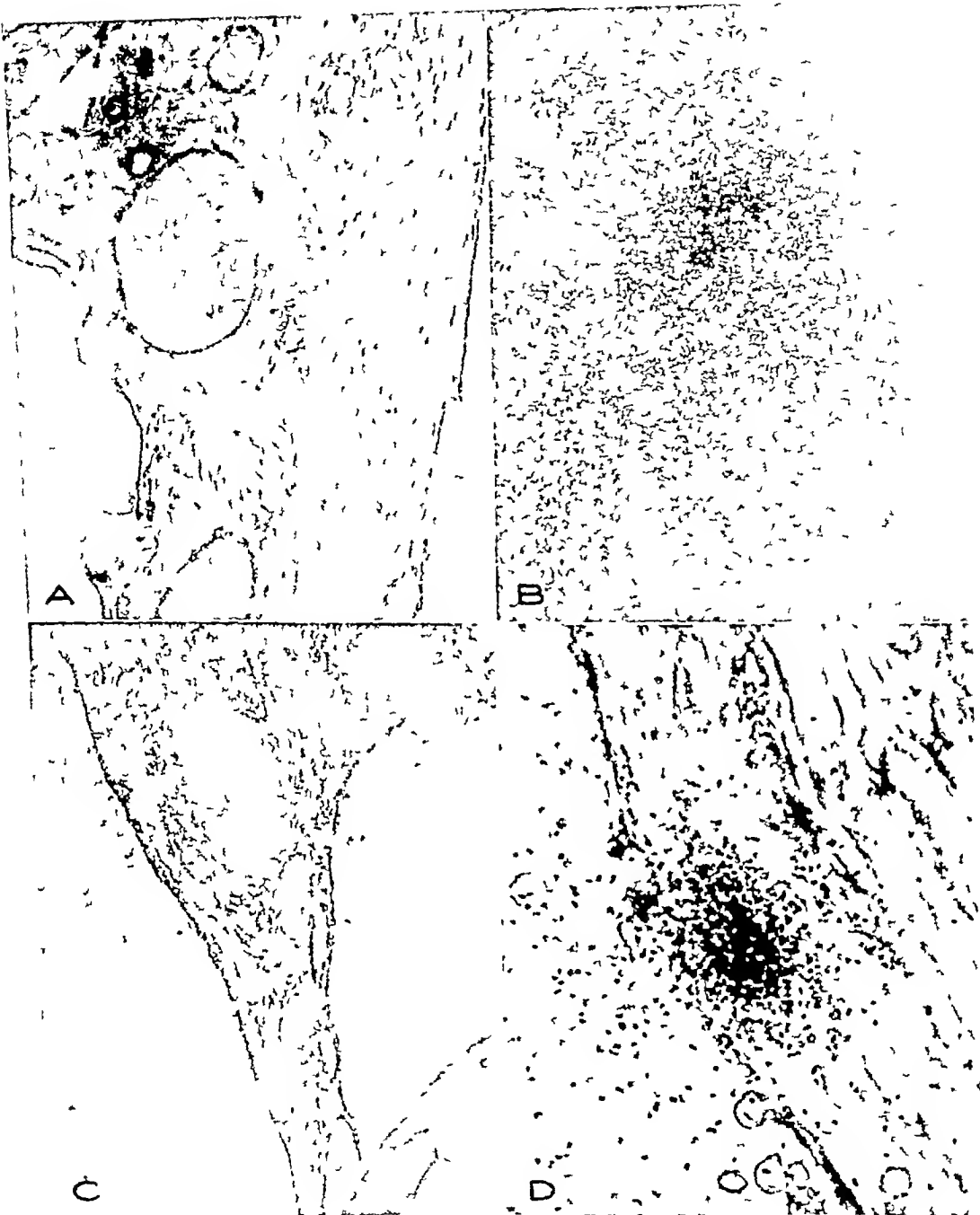


Plate IV. A Photomicrograph of a section of thyroid carcinoma superimposed on the autograph which had been exposed and developed separately. The plane of focus is that of the tissue ($\times c 100$).

B Photomicrograph ($\times c 100$) of same tissue section and autograph as in 4, with the autograph in focus. It may be seen that localization of the reduced silver grains is not good even though the autograph and tissue appeared to match at lower magnification.

C Photomicrograph ($\times c 100$) of preparation in which tissue is mounted directly on photographic emulsion. The plane of focus is intermediate between that of the tissue and of the autograph. It may be seen that localization indicating presence of radioiodine is much better than that shown in A and B.

D Photomicrograph ($\times 640$) of a small region of same tissue as above figures. In this tissue autograph preparation at high magnification the individual grains of reduced silver may be distinguished. An approximation of the resolution attainable with this method may be obtained by using the diameter of erythrocytes present as a scale.

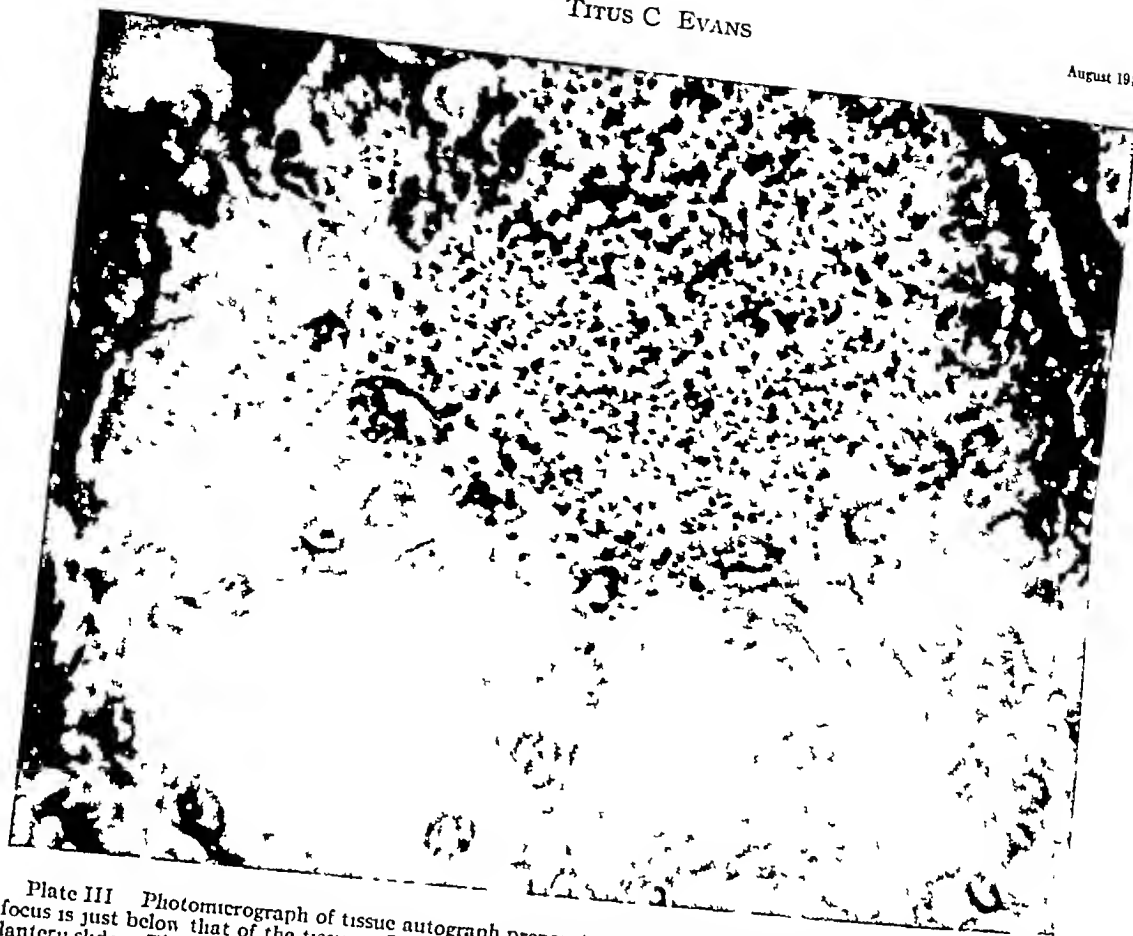


Plate III Photomicrograph of tissue autograph preparation at high magnification ($\times c 950$). The plane of focus is just below that of the tissue. Sections were cut at 5μ and mounted on a 2×2 inch medium contrast lantern slide. The exposure time was seven days. An estimate of the amount of contained radioactivity was obtained by placing a section 2 cm below an unshielded (Technical Associates) beta ray-counting Geiger tube. The activity, with this arrangement was 91 counts per minute.

and the regions of accumulated radioiodine appear to be the same as shown in the autograph (Fig A). As the tissue remains in place on the photographic emulsion, proper alignment is automatic and the tissue-autograph preparation may be examined at higher magnification, as in Fig F, Plate I. The region shown in this figure is that marked with an arrow in Fig C. In order to photograph this region at high magnification, the preparation was turned over so that the thin cover-slip would allow the objective to come close enough to focus on the tissue. Sections shown in B and C were photographed through the microscope slide side in order that the orientation would be the same as in A. Therefore, the left sides of Figs F, and E, are opposite to those of the other

figures in this plate. The follicles shown in Fig F are not the same as those of Fig E but the section is through the same general region. The photomicrograph ($\times 33$) of the tissue-autograph preparation (Fig F) shows that the radioiodine is apparently concentrated in the small follicles and in some of the larger ones. The preparation was made on a lantern slide and stained with Harris' hematoxylin and eosin.

The tissue-autograph preparations may be studied at higher magnification, and as one changes from the low-power objective to the higher power, the plane of the tissue and that of the autograph become more distinctly separate. Both images may be visualized simultaneously by focusing up and down rapidly with the fine adjustment of the microscope. Fig A of Plate II is a

analysis of these cases will be published by the investigators concerned. However, brief mention of some of these observations serves to call attention to the type of detailed information that may be gained by employing tissue-autograph preparations. For instance, it appears that in the adenomas there is some correlation between radioiodine uptake and appearance of the tissue (heavy in growing follicles, diffuse in larger ones, and lacking in degenerating ones). The concentration of radioiodine was less consistent with the appearance of the tissue in the carcinomas. It may be seen in Fig. A of Plate V that some of the follicles concentrated radioiodine and adjacent ones contain much less. In Fig. B of Plate V the concentration of this dose of radioiodine appears not in the region of follicles but in the stroma, where small groups of cells are apparently beginning to function. One should not consider this finding as general, as we have recently examined metastases from another case of thyroid carcinoma in which the more differentiated regions contained the heavier concentration of iodine.

It is evident from the illustrations and the above discussion that tissue autograph preparations will aid in the study of thyroid function and may help in determining

whether a certain case of thyroid neoplasia should be treated with radioiodine.

SUMMARY AND CONCLUSIONS

By mounting the tissue section directly on the photographic emulsion, it is possible to obtain radioautographs which are automatically in alignment with the histologic preparation. This allows, in effect, a differential "staining" of either large or minute regions that have concentrated radioiodine within a certain period of time.

NOTE. It is a pleasure to acknowledge the technical help provided by Miss Grace Clarke, Miss Estelle Sobel, and the other assistants of the laboratory. The writer is also indebted to Dr. G. Failla and Dr. Edith Qumby for their advice and encouragement.

Radiological Research Laboratory
630 West 168th St
New York 32, N. Y.

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SUMARIO

Radioautografías de los Tumores Tiroideos

Las preparaciones histo-autográficas ayudarán en el estudio de la función tiroidea y pueden ayudar a determinar si debe o no tratarse con radio-yodo un caso dado de neoplasia tiroidea.

Montando el corte histológico sobre la emulsión fotográfica es posible obtener

radioautografías que automáticamente alinean con la preparación histológica, lo cual permite, en efecto, la "coloración" diferencial de regiones ya extensas o minúsculas que han concentrado radio-yodo dentro de cierto período de tiempo.

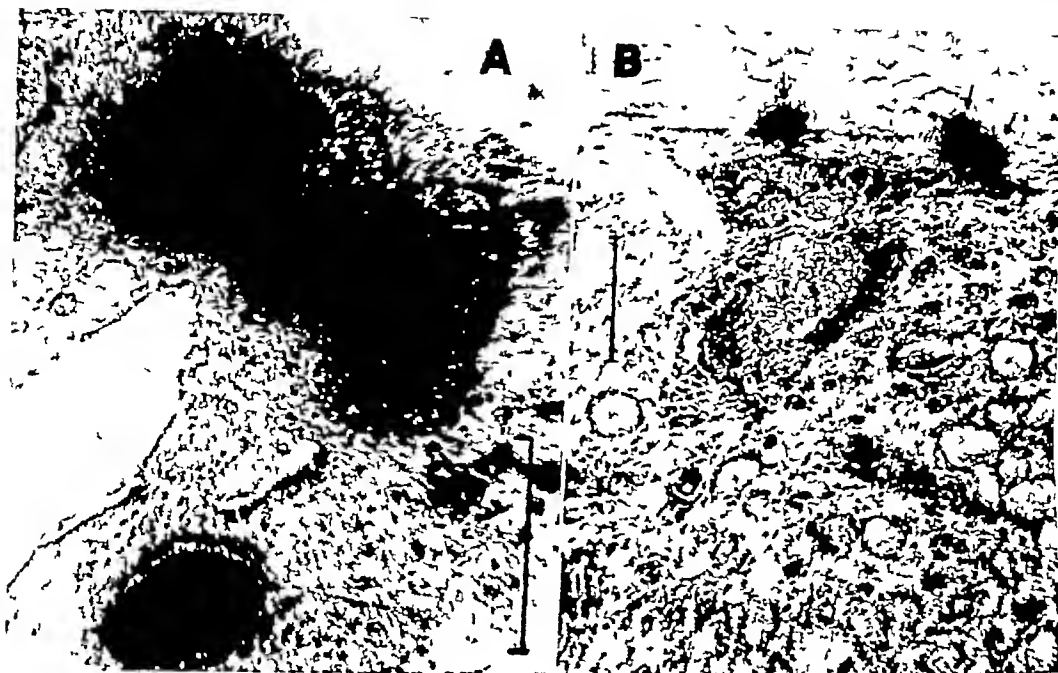


Plate V A Photomicrograph of tissue autograph preparation ($\times 300$ scale 100μ) from tissue taken from a thyroid carcinoma. The plane of focus is intermediate between that of the tissue and that of the autograph. Areas of heavy radioiodine concentration are indicated by the darker regions.

B Photomicrograph of tissue autograph preparation ($\times 160$ scale 100μ) from thyroid-carcinoma metastasis. Regions of accumulated radioiodine are indicated by the arrows.

photomicrograph of a follicle and adjacent tissue from the second case of thyroid adenoma. At this magnification ($\times c 520$), it is not possible to photograph all of the developed grain in the same plane with the tissue. The photograph actually shows a better localization of the grain within the follicle than does the preparation viewed through the microscope. In the microscope field, by focusing up and down, one sees that, although there is a greater concentration of dots under the follicle, there is considerable "background" underneath all of the tissue. Three follicles of the first case are shown in Fig B of Plate II at a magnification of $c 620$. The focus here is just below that of the tissue. The grain appears dense within the follicles and extends with decreasing density beyond their boundary. Plate III shows a small region of an adenoma highly magnified ($\times c 950$). The amount of reduced silver is high under the upper follicle, is slight in the smaller one to the left, and there is practically none in the two lower ones.

Tissue-autograph preparations have been made of two autopsy specimens of thyroid carcinoma sent to us by Dr S M Seidlin, Miss Eleanor Oshry, and Dr A A Yalow of Montefiore Hospital. Examples from the first case are shown in Plate IV. The "regular" autograph presents no distinct pattern, but by superimposing the histologic preparation on the autograph (so that previously made marks on the two coincide) it is possible to obtain satisfactory matching at low magnification. Under slightly higher magnification it is found that the autograph is diffuse, and critical alignment is difficult (see Figs A and B, Plate IV). In the tissue-autograph preparation the alignment remains intact and localization of the radioiodine is evident (Figs C and D, Plate IV).

The "regular" autographs (histologic preparation separate from autograph), not shown in this paper, of the second case of thyroid carcinoma are more distinctive in pattern and serve to check the findings of the tissue-autograph studies. A critical

cer of the prostate demonstrates that a chemical change in the internal environment of the host has brought about a long-continuing regression of a malignant neoplastic process "

As suggested above, it is these and similar reports that have led me to a review of my own cases. First, however, it may be well to say something about the incidence of prostatic carcinoma. According to the statistics of the Metropolitan Life Insurance Co., carcinoma of the prostate accounted for 1.5 per cent of 127,740 cancers in their total number of insured. This figure is in close agreement with that of Randall (16), who found an incidence of 1.3 per cent in a series of 1,215 necropsies. Herzog (9), of Concepción, Chile, believes that 2.25 per cent of all cancers in men involve the prostate, and Moore (12), reviewing the prostatic findings in a consecutive series of autopsies, points out the rising incidence with advancing age. For 229 men dying between the ages of 51 to 90 the figure was 21 per cent.

The high incidence of prostatic carcinoma in older men is explained by the frequent occurrence of malignant change in the hypertrophied prostate. Ewing believed that 33 per cent of men beyond the age of sixty have some increase in the volume of the prostate and quotes various authorities as claiming that 5 to 14 per cent of these enlarged glands undergo malignant transformation (7). In view of these findings, the importance of early operation in prostatic hypertrophy is obvious if we are to forestall the development of cancer. Young is said by Creevy (6) to have found only 3.4 per cent of a series of 1,040 cases of prostatic cancer suitable for radical operation with hope of cure. Among 351 cases, Barringer (3) found only 4.5 per cent in which the cancer was localized to the prostate and periprostatic tissues. Bumpus (quoted by Creevy) discovered bone metastases in 24 per cent of his patients on the initial examination, and Ferguson (8) stated that 30 per cent of his patients came to him with metastatic lesions.

These facts are mentioned in explanation of the high percentage of failures in the treatment of prostatic cancer. Charles Mayo is quoted (11) as saying that, whatever one does, prostatic cancer is incurable, an aphorism which may require some modification in view of the more recent work of Huggins and others (1, 2, 15, 17).

Reports on the use of radiation in the treatment of prostatic cancer have long appeared in the literature. Bumpus, in 1922, reported a series of 217 cases treated with radium applications, but only 8 of this number were alive after three years (5). In 1942, Barringer (4) reported a series of 352 cases treated by some form of irradiation—chiefly implantation of radium needles through the perineum or suprapubically—with a minimum of surgical intervention. Thirty-six (10 per cent) of the patients survived more than five years. Of these, 15 died of carcinoma between the fifth and tenth year, while 21 (6 per cent of the total) were alive and apparently free from cancer after five to nineteen years. In 2 cases (proved by biopsy) coming to necropsy six and seven years, respectively, after treatment, no trace of cancer was found.

Thompson (19) believed that complete surgical removal of even the smallest prostatic cancer is impossible because of its early invasive growth (Kahler, Baron, and August). At the Mayo Clinic, from which his report comes, suspicious nodules are irradiated and kept under observation. When obstruction occurs, transurethral resection is done in addition to irradiation or orchiectomy. Of 877 patients surviving operation (among a total of 887), 206 received irradiation, chiefly by 200-kv roentgen rays. Five-year results were available for only 69 of these patients (treated prior to 1937). Of these, 14.5 per cent were still alive.

The question arises: How can radiation act on a carcinoma composed of such highly differentiated cells as are found in these prostatic neoplasms? In the case of radium implantation, this is easily explained by the cauterizing action of the alpha and

Cancer of the Prostate¹

PROFESSOR DR. LEONARDO GUZMAN

Director of the Institute of Radium, Santiago, Chile

IN VIEW OF THE recent work on the treatment of carcinoma of the prostate by estrogens on the one hand and by castration on the other, sometimes supplemented by irradiation of the suprarenals or the pituitary, the following report of 25 cases treated in the past ten years is presented. Fourteen of this number were proved by biopsy, in the remainder, diagnosis was based on clinical findings.

In a paper presented before the American Urological Association in 1944, Alyea (1) pointed out that, while the good immediate results of castration or diethylstilbestrol in prostatic carcinoma are now established, certain questions remain to be answered. How long will the palliative effects persist? Will the patient live longer and in greater comfort? Are metastases delayed or prevented? Which is to be preferred, stilbestrol or orchiectomy, or a combination of the two? Alyea's own series of cases, treated by orchiectomy, numbered 110 and included 40 in which the operation had been done between two and three years earlier. From his personal observations and a review of reported series, he concluded that life is prolonged and made more comfortable, though palliation is frequently temporary. His last two questions he was unable to answer, but his own preference, so far as treatment is concerned, was for orchiectomy plus small doses of stilbestrol postoperatively to inactivate extragonadal androgens.

Stirling (18), in a paper presented at the same meeting, concluded that, while castration and estrogen therapy seem to be palliative, they neither prevent recurrence nor retard metastasis. Neither procedure, he believed, would completely eliminate androgenic activity.

Munger (13), in a discussion of the foregoing papers, placed testicular irradiation on a par with surgical castration, attributing to each appreciable temporary improvement. He did not consider estrogen alone a sufficient adjunct to these measures. For maximal stabilization he advised regional irradiation to and including the level of the adrenals. Such irradiation, he felt, given coincidentally with the administration of estrogens, enhances the efficacy of their attack on the extragonadal hormonal depots.

Wattenberg and Rose (21) have distinguished between the secretory and growth functions of the prostatic cancer cells, holding that the growth factor is influenced during estrogen therapy by the change in secretory function. The acid phosphatase, which is the enzyme produced by the carcinoma, may fall to a low level following administration of estrogen, with consequent retardation of tumor growth, but sooner or later, even with a diminished secretory function, the growth function will gain momentum. Furthermore, some carcinomas have a low secretory function but an active growth function, and in such cases x-ray therapy will be required.

Huggins (10), five years after the introduction of endocrine therapy of prostatic cancer—in the form of orchiectomy or administration of estrogens—sought to evaluate the results of such treatment. In 18 or 20 cases treated by orchiectomy he obtained remissions of varying duration, though the disease was far advanced, with widespread skeletal metastases and an elevated serum phosphatase. Five patients were alive after five years, 4 with no evidence of tumor, but no claims of cure are made. Huggins concludes merely that "the antiandrogenic therapy of can-

¹ Accepted for publication in December 1946

Eleven radium needles were implanted through the perineum 9 of 40 mm length, containing 2.66 mg each, giving 4.32 mcd, and 2 containing 1.33 mg, giving 0.48 mcd daily. The fact that the needles were arranged in the form of a tetrahedron 1 cm apart, indicates the enormous size of the tumor. They were left in place for seven days, giving a total dose of 33.60 mcd, or 4,468.8 mg hr.

On removal of the needles, the ligneous mass had become soft and was greatly reduced in size, so that treatment with the radium pack was omitted. All symptoms disappeared within a month and the patient was well seventeen years later.

Comment While no histologic proof of cancer was obtained in this case, the experience of the urologists making the original examination was such that a clinical diagnosis can be accepted as reasonably conclusive.² In any event, a patient suffering from serious urinary disturbances obtained relief without operation and was still well after seventeen years. In view of such a result, failure to give radium therapy to advanced prostatic lesions, whether benign or malignant, is a serious omission.

CASE III J V V, age 70, complained of urinary disturbances beginning in April 1929 and increasing in severity until retention occurred in March 1930. Because of severe back pain over a period of six months, he had been treated for lumbago. In April 1930, examination by Dr J Díaz Muñoz revealed an inoperable prostatic growth, the size of a man's fist. On May 3, six radium needles were implanted in the neoplastic tissue, by way of the perineum, giving a dose of 17.28 mcd, or 2,298 mg hr in six days, at the end of which time they were removed. From May 12 to May 14, a radium pack was applied to the hypogastric region for a dose of 12.6 mcd daily. The patient stood the treatment poorly however, and it had to be discontinued. He left the hospital on May 17, at which time urination was easy. Unfortunately cachexia ensued, roentgen radiation could not be given for the severe lumbar pain, and death ensued from bone metastases in September 1930.

Comment While dysuria was relieved in this case, treatment could not be completed with roentgen rays, and generalization of the neoplastic process was not halted. Orchiectomy or irradiation of the testes might have proved useful.

CASE IV E R, age 59, complained of dysuria, retention, and severe pain suggestive of lumbago. He was examined by Drs Díaz Muñoz and Kuschel, who found a greatly enlarged prostate and carcinoma. Cystostomy showed the growth to be even more extensive than it appeared clinically and confirmed the impression of inoperability. Vesical drainage was established, and fifteen days later eight needles of 2.66 mg of radium each (40 mm length, 0.5 mm Pt filter) were implanted through the perineum, being permitted to remain for six days, for a dose of 23.04 mcd, or 3,064 mg hr. Treatment was well tolerated and dysuria was promptly relieved. The spinal metastases were not treated, and the patient died a year and a half later from generalization of the disease.

Comment In this case dysuria was relieved and the patient felt well enough that he did not wish to be treated for what he designated as his bearable lumbago. The final histologic diagnosis (Dr Croizet) was adenocarcinoma.

CASE V G C D, age 59, was seen by Dr Díaz Muñoz in October 1929 with a hard, ligneous pelvic-prostatic mass diagnosed as carcinoma. He gave a history of dysuria since August 1929, culminating in retention. Only in June 1930, however, after repeated episodes of hematuria, was treatment accepted. At that time, six 40-mm needles, each containing 2.66 mg of radium, with 0.5 mm Pt filtration, were implanted in the mass through a perineal incision, being left for a dose of 23.03 mcd, or 3,044 mg hr. Because of the severe hematuria and the presence of urethral nodules, a radium needle (2.66 mg) in a small catheter was introduced into the urethra for seventy-two hours, giving a total dose of 1.44 mcd, or 191.52 mg hr, over a length of 40 mm, a very small intra urethral dose. One month later urination occurred for the first time without catheterization, the prostate began to decrease in size and hardness, and there was a gain of 5 kilos in weight. The patient then left to recuperate in the country and was not again seen until two years and two months later, when he returned with a mass in the left ilio-inguinal region, which was believed to be of the same nature as the original prostatic tumor. The prostate was found on rectal palpation to be in good condition. Irradiation of the inguinal mass (5,100 r) was carried out from Aug. 23 to Sept. 7, 1932. An immediate weight increase (from 59 to 63 kilos) ensued, but in December the patient's condition became worse, and death occurred early the following year.

Comment Biopsy in this case showed adenocarcinoma. In spite of the desperate condition of the patient when treatment was instituted, a substantial improvement

² Dr. Gonzales Rioseco, at the Sixth Surgical Congress, held in Concepción in May 1946 said: "Rectal touch practised by an experienced specialist gives the necessary data for diagnosis." I believe that he is right.

beta particles, leading eventually to fibrosis. In the case of roentgen therapy and distance irradiation from a radium bomb or radium pack, the explanation lies in the fact that so many of these carcinomas develop in hypertrophied glands with an abundant, well vascularized stroma, which responds favorably to irradiation. In the alveolar type of cancer, the alveoli are closed and conglomerated.

Krompecher, according to Ewing (7), included among prostatic neoplasms adenocarcinomas containing basal cells, which are known to be radiosensitive. Herzog (9), quoted above, found that 25 per cent of his cases were a combination of adenocarcinoma and solid undifferentiated carcinoma. There may also be pavement cells in neoplasms arising from the urethral canal in the glands about the bladder neck (called by Coutts "feminoides"), which are not cured by estrogens but do respond to irradiation. Finally, Kaufmann (quoted by Ewing) has described round-cell sarcomas of the prostate. Munger (14) has covered the situation in a general way in the statement that, while most malignant prostatic tumors are adenocarcinomas, and consequently radioresistant, it is noteworthy, nevertheless, that they are decidedly more radiosensitive than the same type of tumor in the digestive tract.

Young (22), in 1913, inspired by the work of Pasteau and deGrais, conceived the idea of a radium-bearing sound for insertion into the urethra. He cited the work of Deming, who demonstrated conspicuous absorption and destruction of cancer tissue following the implantation of radium needles through the perineum or urethra and mentioned a case in which so great reduction in the size of the tumor was effected that radical operation became possible and the patient was well eleven years later. "This fortuitous case," wrote Young, "would seem to indicate that radium should be employed more frequently in an effort to make some of these cancers curable by the radical operation." I myself presented before the Sociedad de Cirugía of Santiago, Chile, in person, a

patient who had been treated by perineal implantation of radium needles sixteen years earlier. Young mentions briefly roentgen therapy as being effective in some cases of extensive carcinoma.

The more recent use of radiation in carcinoma of the prostate has been in association with orchietomy or roentgen castration, as mentioned above.

CASE REPORTS

CASE I A M, age 56, was operated upon in May 1928 by Dr Coutts for cancer of the prostate. A nodule about the size of a hazelnut, invading the right lobe and involving the seminal vesicle on that side, could not be removed. The histologic diagnosis was alveolar adenocarcinoma.

Following operation, hematuria and frequency continued, and examination in September 1928 showed invasion of the right half of the pelvis. On Sept 12, radium therapy was begun. Five long needles of 1.33 mg each, with 0.5 mm Pt and 1.0 mm brass filtration, were implanted through the perineum into the nodule surrounding it and left for five days for a dose of 6.25 mcd (831 mg hr). On the day of their removal, a radium pack (six 10-mg tubes with 2.0 mm Pt filtration) was applied to the hypogastric region at 4.0 cm distance from the skin and left in place for fifteen days, completing a dose of 162 mcd (21,546 mg hr).

By Oct 15, the urethral obstruction, hematuria, and frequency had disappeared, the affected lobule had flattened, and the patient was able to sleep from 11 P M to 5 A M without urinating. The only complaint was sexual impotence. There was no further change until the beginning of 1931, when the condition suddenly became worse and death from recurrence ensued.

Comment In this case life was prolonged in comfort for more than two years. Besides the local action of the radium implanted in and around the mass, there was irradiation of the pubic region, since it is difficult to filter adequately a mass of 60 mg of radium. Thus, unintentionally, the testes were irradiated with gamma rays in accordance with the procedure more recently recommended by Munger.

CASE II A D, age 60 was seen by Drs J L Bisquertt and Correa in November 1929 with a hard, nodular, inoperable tumor of the prostate adherent to the rectum, diagnosed clinically as cancer. The patient had had a right orchitis of unknown origin in October 1928. In March 1929 he began to experience difficulty in urination and nocturia and in May of that year retention occurred.

Muñoz and Dr. Donoso Barthet revealed a prostatic-pelvic carcinosis. A course of irradiation—7,000 r—was given to the pelvis from May 15 to June 20, through six fields. The patient felt much improved until October, when a phlebitis of the left leg developed with severe pain in the lumbar region. "Cobrina" was injected without effect. Death from cancer ensued in November.

Comment This case is an example of a far advanced lesion of a high degree of malignancy. Relief of dysuria was of only four months' duration.

CASE XI A C, age 63, had experienced urinary obstruction since April 1935. In October of that year he consulted Professor Bisquertt, who on examination discovered an indurated, ligneous mass shaped like the head of an ox, with the seminal vesicles forming the horns. Cystostomy was done and radium was implanted transperineally—seven needles of the type previously described—for a dose of 26.88 mcd, or 3,575 mg hr, over eight days. By December the prostatic mass had disappeared except for slight induration of the left vesicle. Failure of the cystostomy to close led the patient to refuse further treatment with roentgen rays; the left vesicle continued to increase in size and, in spite of palliative measures, death occurred in January 1937. Biopsy showed adenocarcinoma.

Comment The vesical disturbances having been relieved in this case and the prostate greatly reduced in size, I believe external irradiation, as in Case I, might have been useful.

CASE XII C A B, age 70, was operated upon in June 1934 by Dr. Coutts for carcinoma of the prostate. Extirpation was impossible, however, as the entire capsule was invaded and indurated. Dysuria, which had been present since the end of 1933, went on to obstruction. The patient was again examined in May 1935, when an indurated mass the size of an orange was present. Hematuria had also appeared. Irradiation to the hypogastrium was begun on May 6, 1935, with a radium pack⁴ consisting of ten 10 mg tubes at 5 cm from the skin. A dose of 180 med, or 23,940 mg hr, was given in ten days. The urinary output increased from 800 to 2,500 cc daily, and the patient, previously prostrated, was able to be up. During July he received additional radiation to the pelvis—5,000 r. He continued to feel well till January 1936, when severe pain in the spine developed. There was no recurrence of dysuria, but spinal metastases had evidently occurred, and death followed in March 1936. The biopsy diagnosis was adenocarcinoma.

⁴ Columbin paste (Esguerra, Regnaud, Monod, Lacrosgue).

CASE XIII A H, age 78, was operated on for prostatic adenocarcinoma, proved histologically, on June 26, 1931. In January 1936, hematuria and urinary difficulties developed. At that time, an indurated prostatic mass, 7 cm in diameter, was found, and indurated seminal vesicles were also palpated. From March 3 to April 17, 8,000 r were delivered to the pelvis. The mass was greatly reduced in size, hematuria ceased, and the patient's general condition improved. He was followed for two and a half years.

Comment X-rays in sufficient dosage served to keep this patient well for at least two and a half years. Undoubtedly the testes received some radiation, which may have contributed to the good result.

CASE XIV W E, age 60, was seen about the middle of 1937 complaining of impotence, constipation, and loss of weight (15 kilos) but *not of dysuria*. In the right iliac fossa was a ligneous indurated mass the size of a fist. Routine examination revealed, also, a hard prostate, about the same size. Suspecting a prostatic lesion, I sent the patient to Professor Bisquertt, who made a clinical diagnosis of prostatic carcinoma, with invasion of the hypogastric and iliac lymph nodes. Roentgen therapy was given from Sept. 27 to Oct. 10—8,000 r through three 10 × 10 cm fields to the abdomino-iliac mass and an equal amount through five fields to the region of the prostate. The factors, as in the other cases, were 200 kv, 10 ma, 20 mm Cu filter, 80 cm distance.

Following treatment the patient showed a remarkable improvement, working as he had never worked before as head of a large industry. He remained well for two years. In July 1939 he was again examined. The prostatic and abdominal masses had disappeared, and there had been an increase of 16 kilos in weight, but there was evidence of spinal metastasis. Roentgen therapy to the spine was given for thirty days for a total dose of 3,500 r, liver extract being injected to avoid anemia. The pain was relieved and the patient returned to his work for another year. In October 1940 tetraplegia developed and there was evidence of osteoblastic metastases even in the cervical spine. Roentgen irradiation afforded slight palliation but cachexia supervened, with death in January 1941.

Comment In this case we have an example of prostatic cancer without urinary symptoms. The patient lived three years in excellent condition, able to carry on his work. The question arises as to what effect the radiation had upon the gonads. I believe that it exerted some effect, since the patient remained impotent after his

was obtained for a period of two and a half years, which compares favorably with the results of the treatment now in vogue. It is of interest that the patient's wife was seen in 1934 with a squamous-cell epithelioma of the urethra, which is being treated by radium.

CASE VI L A M, age 50, had an indurated, ligneous, irregular prostate the size of an orange. He gave a history of dysuria since 1929, culminating in sudden retention following a heavy meal and excessive drinking. The patient had been under the care of two specialists and had undergone bladder irrigations. According to his statement, he became worse on one occasion following this procedure and a month later expelled a mass of hair.² On Feb 23, 1931, eight radium needles, 40 mm long, of 2.66 mg each with 0.5 mm Pt filtration, were implanted through a perineal incision—four in each lobe of the prostate. A dose of 30.72 mcd, or 4,085.76 mg hr, was given in eight days. This treatment was well tolerated but the patient would not consent to further irradiation with the radium pack or roentgen rays. The mass in the prostate diminished in size, but pain and tenesmus continued, cachexia developed, and death occurred in 1931.

Comment This is the only case in which some relief of vesical complaints was not obtained. We explained this failure on the hypothesis that the tumor was a radio-resistant teratoma.

CASE VII J C G, age 68, was seen in July 1928 in Professor Bisquertt's clinic with cancer of the prostate, proved by biopsy. The gland was the size of an orange, ligneous, indurated, and irregular. Eight 2.66 mg needles were implanted for seven days, giving a total dose of 26.88 mcd or 3,575 mg hr. Dysuria was relieved and the patient was well up to June 1931. At that time the prostate was reduced in size but a tumor had appeared in the left iliac fossa and there was severe pain in the sacrum radiating toward the left thigh. The patient was also suffering from diabetes. Roentgen therapy was advised but refused, cachexia developed, and death ensued in December 1931.

Comment This is another example of three-year survival in relatively good health. As in other cases, by means of a simple procedure almost as much was accomplished as could have been achieved by

² This suggested to me the possibility of a dermoid cyst. Ewing discussing dermoid cysts of the pelvic connective tissues wrote: "The presence of hair in the evacuation has been the first symptom observed or the bladder can be invaded and hairs can appear in the urine."

orchiectomy, without the production of emotional or mental disturbance.

CASE VIII D B, age 64, had been quite well until March 1932, when, following coitus he noticed blood on the meatus. Subsequently hematuria occurred and on examination a hard, irregular prostatic growth was discovered, which had already extended beyond the capsule. As the tumor was considered inoperable, suprapubic cystostomy and perineotomy were done, as in Case IV (a procedure described as recently as 1936 by Chauvin). Four 40 mm radium needles of 2.66 mg, 0.5 mm Pt filter, were implanted in the prostate and one, in a catheter, in the urethra. Seven days later the needles were removed, having delivered a dose of 13.44 mcd, or 1,787.52 mg hr, to the tumor and 3.36 mcd, or 446 mg hr, in the urethra. 4 weeks later the cystostomy was closed, a catheter being left in place for three days longer. Hematuria ceased. Roentgen therapy was then given—4,200 r in twelve sessions (June 1932). The patient remained in good condition with no impairment of sexual potency, until June 1942, when severe pelvic pain developed. Castration and transurethral resection were then done by Dr Bernardo Lira with out affording relief. I saw the patient in January 1943 in very poor condition. Roentgen irradiation of the lumbar spine and sacroiliac region was without effect and death occurred a month later.

Comment This patient, with a carcinoma of the prostate, proved histologically, lived for ten years in good condition. We do not believe that an equally good result could have been obtained with castration and estrogen therapy.

CASE IX Dr D gave a history of dysuria and lumbar and sacroiliac pain. His prostate was enormously enlarged, indurated, and ligneous to the touch. He would not permit implantation of radium needles, and roentgen therapy was instituted. After ten treatments, during which a total dose of not more than 2,500 r was given, further irradiation was refused and death from cachexia ensued a few months later.

Comment In this connection, it may be said that physicians frequently believe that it is the same thing to apply 1,000 r and 8,000 r, for example, and that treatment is the same for all cases. They fail to appreciate that radiotherapy, like such drugs as penicillin and the sulfonamides, must be given in appropriate dosage and at suitable intervals.

CASE X G R C, age 64, was seen in 1934 complaining of dysuria. Examination by Dr Díaz

large and indurated. As the condition was inoperable, roentgen therapy—7,000 r—was given to the pelvis in 1939. After a year and a half, during which the patient remained in good condition, he returned with a recurrence. Roentgen therapy was again given—4,500 r, and in February 1943 a third series was given for a further recurrence. The patient remains well. There was no biopsy in this case, but the clinical diagnosis is considered reliable.

CASE XXIV C D, age 53, suffered from dysuria from 1941. In December 1942, episodes of massive hematuria occurred at the beginning and end of micturition. Examination in 1943 by Professor Bisquertt revealed a large, indurated, irregular prostate. Cystoscopy showed small bleeding outgrowths on the bladder neck. There had been a loss of 6 kilos in weight. Estrogens were without effect and I therefore undertook to irradiate the lesion and the testicles (July 3–Aug 15, 1943). Dysuria at first became worse but began to improve during the fourth week of treatment, hematuria ceased, and the prostatic mass disappeared. There was a gain in weight of 14 kilos. In the last two years acid phosphatase determinations on two occasions have been normal.

CASE XXV D H, age 62, underwent transurethral resection in 1943. He remained well until April 1945, when hematuria and dysuria recurred and his general condition declined. I attempted to irradiate the testicles and prostate in June 1945, but the patient was extremely nervous and toxic so that no regularity of treatment could be observed. Only 2,000 r were given. The condition failed to improve and death occurred from cancer.

SUMMARY OF CASES

We have here 25 cases of cancer of the prostate, of which 14 (I, IV, V, VII, VIII, XI, XII, XIII, XVI, XVIII, XIX, XX, XXI, XXV) were proved histologically, while the others gave undoubted clinical evidence of malignant growth. Case VI was presumably a pelvic dermoid cyst. With this one exception, every patient receiving adequate radiation experienced prompt relief of dysuria for varying periods. In each instance there was marked diuresis following treatment.

One patient (Case II) has lived seventeen years in good condition, *i.e.*, six years longer than the patient mentioned by Young (22). A survival period of ten years was obtained in Case VIII. In Case XV death from bronchopneumonia occurred four years after relief of dysuria by

roentgen therapy. In Case XXIII the survival period has reached five and a half years with recurrences at a year and a half and again two years later. The patient is without urinary symptoms at the time of this report. Still another patient (Case XX) is without symptoms three years and ten months after the first treatment, a recurrence having been treated in the interval by irradiation to the pelvis.

In 5 other cases (I, V, XIII, XIV, XXIV) dysuria was relieved for periods from two and a half years to over three years. In Case XVIII relief from dysuria had continued for two years when the patient was last heard from, and in Case XII dysuria disappeared for ten months. Briefer periods of relief were obtained in the remaining cases, in which complete treatment could not be given.

CONCLUSIONS

We are in agreement with Barringer that treatment of prostatic carcinoma with radiation will relieve dysuria and prolong life in comfort. We believe that the results compare favorably with those of transurethral resection, which was reported by Thompson and Emmett (20) as giving 74 per cent of one-year survivals in a series of 253 cases, 46 per cent two-year survivals, 31 per cent three-year survivals, 17 per cent four-year survivals, and 8.7 per cent five-year survivals.

We believe that before instituting treatment for any case of prostatic carcinoma, the method of choice for that case should be determined, whether transurethral resection, irradiation, or castration with or without estrogens, or some combination of these procedures.

We believe irradiation is most useful in reducing the volume of the primary tumor and relieving pain due to metastases. If estrogens and castration fail, as they may in tumors arising in the periurethral glands, radiation can still be employed.

We agree with Munger that adequate testicular and regional irradiation diminishes hormone production (by regional

first treatment No biopsy was done in this case

Incidentally, the wife of this patient was seen in 1943 with a pavement-cell epithelioma of the cervix She is now (1947) without evidence of cancer following radium therapy (Regaud method)

CASE XV U B, age 69, gave a history of urinary difficulties since the age of forty, becoming worse in the last two years On examination, Professor Bisquerri found an indurated prostatic mass invading the seminal vesicles The clinical diagnosis was prostatic cancer arising in an old adenoma No biopsy was done As the condition was regarded as inoperable, x-ray therapy was given in July 1939—8,000 r in 30 sessions, with the factors described in the cases recorded above After a month the urinary symptoms disappeared The patient's general condition improved, and he lived until 1943, when he was reported to have died of bronchopneumonia

CASE XVI C M, age 74, was first seen by me in December 1939 He had been operated on in 1937 for prostatic carcinoma (proved histologically) Metastases were now present in the 4th cervical vertebra and the 6th left rib, and there was a local recurrence in the left half of the true pelvis Roentgen therapy was given to the metastases and pain disappeared Only 3,500 r were given to the pelvis, as we feared to use a larger dose because of the possibility of anemia, in view of the patient's age and the fact that the short bones had been irradiated After eight months of well-being, death occurred from pneumonia

Comment In spite of the relief following treatment, I believe that the local recurrence in this instance continued to progress This would have been an appropriate case for orchiectomy

CASE XVII F W, age 76, was seen by us in August 1940, with a history of dysuria for five years, becoming more severe in the past six months, with loss of weight and pelvic pain He had undergone section of both spermatic cords in 1934 for a bilateral recurrent epididymitis At that time there were 300 cc of residual urine Professor Bisquerri found a large irregular prostate, fixed by ligeneous adhesions As the condition was regarded as inoperable, deep roentgen therapy was given—4,500 r in 18 sessions Improvement followed and plans were made for the implantation of radium through the perineum Unfortunately an indiscreet relative told the patient that he was suffering from cancer and he committed suicide

Comment This tragic case carries its own lesson In our Institute we never

speak of cancer My patients know that I am a specialist in that disease, but so long as there is any doubt of its presence they remain hopeful and give us the co-operation that is so necessary

CASE XVIII G Q, age 55, had suffered from hematuria and dysuria in 1934 He was examined in July 1941 by Professor Bisquerri, who found a greatly hypertrophied prostate with indurated nodules and invasion of the left vesicle A perineotomy was done on Aug 21, 1941, and radium needles were inserted for a dose of 20 16 mcd, or 2,681 mg hr, in seven days As we were not sure that adequate radiation had been delivered to the seminal vesicles, roentgen therapy was given to the pelvis—3,000 r The patient was followed for two years The biopsy diagnosis was adenocarcinoma and prostatic hypertrophy

CASE XIX J D C, age 76, had suffered from progressive dysuria since the end of 1940 The prostate was large and indurated Perineotomy was done on Aug 28, 1941, and six radium needles were implanted, being left in place for nine days, giving a dose of 25 92 mcd, or 3,447 mg hr Dysuria was relieved and when the patient was examined two years and nine months later, he was quite well The biopsy diagnosis was adenocarcinoma

CASE XX J L, age 66, suffered from dysuria from the beginning of 1941 Examination revealed a large, indurated, inoperable prostate Seven radium needles (2 66 mg) were implanted in the prostate transperineally and left in place from Dec 23 to Dec 31, 1941, for a dose of 26 88 mcd, or 3,570 mg hr Urinary symptoms disappeared until May 1945, when the prostate again increased in size and retention developed Roentgen therapy to the pelvis, including the gonads, was then given, 7,000 r being delivered through six fields in thirty sessions Fifteen days later catheterization was no longer necessary The biopsy diagnosis was adenocarcinoma

CASE XXI S C, age 70 gave a history of dysuria for the past year The prostate was large, indurated, ligeneous, and inoperable Radium was implanted (Feb 19–23, 1943) as in the previous case, and a month later catheterization was unnecessary This patient was followed for only six months The histologic diagnosis was adenocarcinoma

CASE XXII F N, age 78, had dysuria and retention for about a year Operation could not be undertaken because of the advanced age and poor general condition Roentgen therapy was given, including the gonads, but when the patient was last heard from retention was still present

CASE XXIII M B, age 71, consulted Professor Lobo Onell because of dysuria The prostate was

Application of Radioactive Isotopes to the Study of Radiation Effects in Cells

MARTIN D. KAMEN, Ph.D.

Edward Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, Missouri

NOTABLE AMONG the fundamental contributions due largely to the availability of tracer isotopes is the concept of the dynamic state of cellular constituents. The structural and metabolic components of the cell are involved in a constant flux of rapid reactions, as shown so convincingly by Schoenheimer (1) and others. Biochemical entities such as proteins, fats, and carbohydrates are linked by simultaneous anabolic and catabolic processes through a "pool" of relatively small atomic groupings which originate from no particular source but are contributed by all cellular materials, structural or otherwise. Despite this seeming welter of reactions, regulation mechanisms in normal metabolism are so efficient that cells and organs remain constant in total amount and composition. Cellular dysfunction and disease processes involve disturbances in these regulation mechanisms. That the chemical nature of these mechanisms has remained obscure is due in no small measure to the lack of a technique for following the exchange of reactive atomic groupings in systems which exhibit no over-all changes in chemical composition. It is in the study of regulation mechanisms in such systems that labeling techniques utilizing tracer isotopes can be expected to make many important contributions. It follows that research into changes in cell metabolism brought about by absorption of radiant energy will be expedited and enriched by knowledge gained with such techniques.

The responses of living cells to radiation are as diverse as the cells themselves. Photosynthetic organisms are so adapted to radiation that they prefer it for efficient cellular synthesis. From this extreme,

the known complex of living systems exhibits responses less and less beneficial until the extreme of lethality is reached. It is evident that before a full understanding of radiation effects is possible it is essential to know in detail (a) the nature of the anabolic synthetic processes obtaining in the absence of radiation, (b) the nature of the foreign constituents introduced by irradiation of the cellular nucleus and cytoplasm, (c) the interaction of these foreign constituents in terms of competitive interaction with the normal metabolites for synthetic material. In this paper there will be reviewed a few researches which appear to be significant in that they suggest one kind of approach to these problems.

Hevesy and his co-workers (2) have applied radioactive phosphorus (P^{32}) in studying the effect of x-rays on cellular division. The particular advantage of using the tracer isotope in these investigations is that there is afforded a means of investigating changes in tissues which have reached full growth. The usual method of mitotic counts is applicable only to growing tissue. A convenient direct method for ascertaining cellular responses or change in metabolic turnover in full-grown tissues is afforded by studying the rate of synthesis of desoxyribose-nucleic acid before and after irradiation. The basic importance of this moiety in cellular synthesis has been suggested by numerous investigators (Caspersson, 3, Brachet, 4, and others).

A specific example may be cited from the researches reported by von Euler and Hevesy (5). When labeled inorganic phosphate is administered to rats im-

¹ Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill. Dec. 1-6, 1946.

irradiation we mean irradiation to the lumbo-aortic and suprarenal regions)

We believe that irradiation should be given not only to the testes and the pelvis, but to the suprarenals and hypophysis to eliminate all extragonadal sources of androgen

Finally, we believe that nothing takes the place of early diagnosis, permitting radical operation without undue risk

Av. Santa Maria 0170
Santiago, Chile

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SUMARIO

Cáncer de la Próstata

Veinticinco casos de cáncer prostático fueron tratados por medio de la irradiación (principalmente en forma de radio por vía intersticial, con o sin irradiación externa con compresas de radio o rayos X) Con la sola excepción de un enfermo en que se creyó había un quiste dermoideo, todos los que recibieron tratamiento adecuado obtuvieron rápido alivio de la disuria. Un enfermo vivió 19 años en buen estado, otro 10 años y otro cinco años y medio, durante los cuales tuvo dos recurrencias que exigieron nueva irradiación. Un enfermo falleció de bronconeumonía cuatro años después del alivio de la disuria, y otro estaba sin síntomas tres años y medio después, habiendo entre tanto recibido irradiación con motivo de una recurrencia.

En 5 casos hubo alivio de la disuria durante dos años y medio a tres años, obteniéndose alivios más breves en los casos restantes.

De lo anterior dedúcese que el tratamiento del cáncer prostático con la irradiación aliviará la disuria y prolongará la vida en comodidad, comparándose favorablemente el resultado con el obtenido con la resección transuretral, que la irradiación es de la mayor utilidad para reducir el volumen del tumor primario y aliviar el dolor debido a las metástasis, que la adecuada irradiación testicular y regional es útil para mermar la hormonogénesis, y por fin, que nada suplanta al diagnóstico temprano, que permite llevar a cabo la operación radical sin correr demasiado riesgo.

The work on nucleic acid turnover under conditions of irradiation is most suggestive when compared with work on various cellular processes modified by chemical agents. Most striking is the action of mustard gas and its nitrogen-containing analogues, the β -chloroethyl amines, on the structure and function of chromosomes (7). It has been shown that in *Drosophila melanogaster*, exposure of adult male flies to sublethal doses induces a high incidence of sex-linked lethals much in excess of the number to be expected on the basis of the natural mutation rate. Horowitz (8) and his co-workers, in confirming and extending the original observations of Auerbach (7) and others, have shown that the mustard gas-induced mutations are remarkably similar to those observed following γ -ray irradiation.

Chemical effects may be associated with a range of energies up to 100 kilocalories, which is not far removed from the energies liberated by absorption of ultraviolet radiation (4-5 electron volts). X-rays release considerably more energy per unit of absorption, so that γ -ray effects may be expected to introduce more intense dislocations of the cellular chemical pattern. On the other hand, the results obtained with the mustards indicate that both types of cellular disturbance may funnel into a common pathway. In this connection, it should be remarked that a link between the energy region of γ -rays and chemical agents has been provided to some extent by the observation of Latarjet (9), who has shown that both ionization and molecular activation can induce the same chemical changes in the same sensitive cellular zone. The absorption of a given quantity of energy, whether delivered by γ -ray photon or by many ultraviolet photons, leads to the same amount of cellular inactivation. In these experiments, Latarjet measured the energy required to produce such effects as the inactivation of bacteriophage, sterilization of dysentery bacillus, and the sterilization of yeast. It appears that the accumulation of energy as molecular activation delivered in small packets by ultraviolet photons can give the same effect as a

single higher energy event (ionization) obtained by absorption of a single γ -ray photon.

On the basis of these results it is not implausible that the induction of cellular dysfunctions such as cancers and leukemias may involve a common metabolic pathway whether the causative agent is radiation or a chemical. It is important therefore to inquire into the normal mechanisms prevailing in the cell for protein synthesis, particularly as mediated by the enzymes present, the substrates they require, and the relation of these enzyme populations to the nuclear genes. Spiegelman (10) has summarized recently the evidence for a theory linking genes in the cellular nucleus with enzymes in cytoplasm through a bridge of self-duplicating nucleoprotein units to which the term "plasmagene" is applied. According to this theory, the genes in the nucleus continually produce replicas of themselves which are ejected into the cytoplasm. These units or "plasmagenes" are assumed to be nucleoprotein in nature and possess varying degrees of capacity for self-duplication. The plasmagenes determine the types and amounts of protein and enzymes synthesized, each plasmagene competing with the others for cellular protein. It is supposed that heritable changes in the ultimate cellular composition can be initiated and maintained by varying the substrate to which the plasmagenes are exposed. This concept of cytoplasmic inheritance interprets a process such as cancer as due possibly to a mutation in a plasmagene, resulting in a new plasmagene foreign to the cell. This plasmagene mutant is enabled to compete successfully for protein and thus interfere with the ultimate development of normal cellular function. Such a concept provides an explanation for the appearance of a sudden heritable change in somatic cells, a phenomenon which appears to be typical of the cancer process (11).

With such considerations in mind, an inquiry into the nature of the chemical processes involved in enzyme synthesis has been started by Dr. Spiegelman and

TABLE I RATIO OF NEWLY FORMED DESOXYRIBOSE NUCLEIC ACID PRESENT BEFORE AND AFTER IRRADIATION IN ORGANS OF YOUNG RATS DOSE 2,000-2,250 r (AFTER HEVESY)

(Time of Experiment 2 hours)		
Organ	P^{32} Administered After Irradiation	Irradiated Throughout Experiment
Liver	2.3	11
Spleen		5.3

planted with Jensen's sarcoma, it is found that the labeled phosphate enters the sarcoma fairly rapidly. In two hours the inorganic phosphorus of the sarcoma is found to contain nearly the same amount of labeled phosphorus as that in the circulating plasma phosphate. Thus the specific activity which gives the amount of P^{32} per milligram of total phosphorus is roughly the same in these two fractions after a lapse of a few hours. It is known from tracer studies that the phosphate bound in nucleic acid and nucleoprotein cannot interchange with inorganic phosphate as such but can make its appearance in nucleic acid only by actual synthesis into the nucleotide. Consequently, the appearance of labeled phosphorus in the nucleic acid fraction gives an index of newly synthesized nucleic acid. The ratio of the specific activities of cellular nucleic acid and plasma phosphate reveal the percentage of nucleic acid synthesized during the interval between administration of the labeled phosphate and the end of the experiment. This synthesis in Jensen rat sarcoma corresponds to an average of about 2 to 3 per cent in two hours. X-ray irradiation of the sarcoma reduces the synthetic activity markedly as compared with the normal rate. More important is the observation that inhibition of synthesis is less marked when studies are conducted with labeled phosphate administered sometime after irradiation. Thus, when labeled phosphate is injected during irradiation lasting two and one-half hours, the total dosage being 2,250 r, the synthesis of desoxyribose-nucleic acid is diminished to one-seventh of the normal value, whereas if the labeled phosphate is administered a short

time after irradiation, the normal rate is decreased only by about one-half.

In normal tissue much the same effects are observed. In Table I, taken from Hevesy's paper (2), there are shown data on the ratio of newly formed desoxyribose nucleic acid in the organs of young rats before and after irradiation. It is seen that when the rat is exposed to x-rays throughout the experiment there results a greater inhibition of nucleic acid synthesis. These data are obtained with rapidly growing animals. In the liver and spleen of adult rats, the synthesis of nucleic acid is found to be many times smaller than in the corresponding organs of young rats, as would be expected. However, the x-ray inhibition of nucleic acid formation is about the same whether the tissues are growing actively or not. The inhibitory effects of x-rays as evidenced by nucleic acid formation are much less pronounced if, instead of sacrificing the animal immediately after irradiation, the inhibition is observed several hours after the termination of irradiation. The experiments of Hevesy and his co-workers indicate that about 75 per cent of the x-ray inhibition is counteracted in two hours after irradiation.

These results, particularly those involving the time factor, are consistent with the notion that there is an interaction of chemical agents produced by x-rays with the cellular constituents mediating protein synthesis and cellular growth. A striking experiment bearing on this point may be cited from the work of Ahlstrom, von Euler, and Hevesy (6). Rats were inoculated with two sarcomas, one of which was subjected to irradiation up to 2,000 r, the other being shielded. The two sarcomas on a single rat were connected only through the circulatory system of the animal. Nucleic acid formation, as evidenced by use of labeled phosphate, was inhibited in the shielded sarcoma almost as much as in the sarcoma irradiated directly. This indicates the production of a diffusible factor in tissue under irradiation which can influence unirradiated cells. The nature of this factor remains to be elucidated.

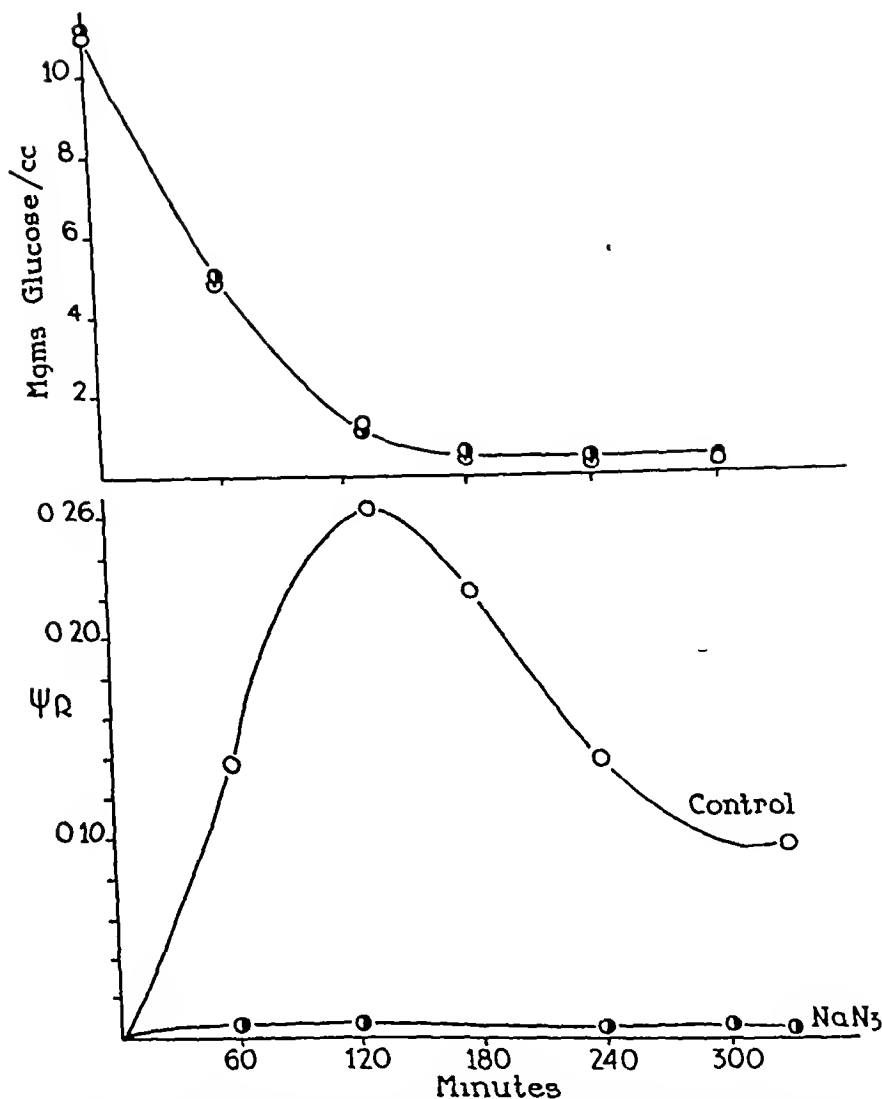


Fig 1 Phosphate turnover in presence of azide. The upper curve represents decrease in glucose concentration of medium as function of time. It is seen that both azide treated and control organisms ferment glucose at the same rate. In the lower curve the ratio of specific activities (P^{32}/P^{31}) in cell phosphate and extracellular phosphate is plotted against time. Equilibration is rapid in the control cells, reaching a maximum just before all glucose is exhausted, after which the ratio drops because of breakdown of newly synthesized intracellular organic phosphate and loss to medium. Little equilibration occurs in the presence of azide.

phosphorus, indicating some flow into this fraction. These data showed unambiguously that rapidly metabolizing but non-dividing cells lost no phosphate from the "nucleoprotein" fraction even though there was a rapid equilibration of the remaining cellular phosphate.

The cells obtained from these experiments now contained a "nucleoprotein" fraction with a specific activity almost four

times as great as the acid-soluble phosphate fraction. They therefore constituted good test material for further study of P-exchange between acid-soluble and "nucleoprotein" fractions. Long periods of fermentation (up to six hours) failed to change the total P^{32} content of the "nucleoprotein" fraction, although the specific P^{32} content declined somewhat owing to dilution by flow of low-specific activity phosphate from

the writer. Some preliminary results using tracer phosphorus are of interest in connection with the problems which are discussed above.

Of necessity, the initial problem in enzyme synthesis must be that of the energy sources and substrates for the synthetic reactions. It will be recalled that in the normal anaerobic fermentation of glucose by yeast cells a portion of the glucose is assimilated into cell material. Inclusion of sodium azide in the medium in concentrations equal to 2.5×10^{-3} M, results in abolition of assimilatory activity, although the rate of fermentation is not affected. Under proper conditions, this chemical agent can inhibit a large variety of cellular functions involving synthesis, i.e., enzymic adaptation, differentiation, ammonia assimilation, etc., although over-all rate of metabolic activity is not changed. From the fundamental and brilliant research of the Coris, Warburg, Meyerhof, Parnas, and others, it may be suspected that the action of azide on mobilization of phosphate for synthesis of organic phosphate esters as synthetic intermediates may be involved. Therefore, we have begun by comparing the distribution of phosphate in the various cellular fractions as influenced by synthetic activity. By the use of azide and tracer phosphorus (P^{32}), it has been possible to study the flow of phosphate between various cell fractions while cellular material is or is not being synthesized and while the over-all utilization of carbohydrate is maintained constant.

In the initial experiments, yeast cells were suspended in a medium containing P^{32} labeled inorganic phosphate. Samples of the cells were withdrawn at intervals during fermentation of glucose and analyzed chemically and by radioactive assay. A typical experiment gave results shown in Figure 1. In this experiment 2×10^{-3} M NaN_3 was used. From the upper curve it can be seen that the azide did not affect the ability of the cells to metabolize glucose, since both the treated and untreated cells consumed glucose at the same rate. How-

ever, the control cells equilibrated organically bound phosphate rapidly whereas the azide treated cells did not. From this type of experiment it seemed reasonable to conclude that azide prevented the accumulation of organically bound phosphate. On the other hand, dinitrophenol, another agent capable of preventing synthesis while not inhibiting over-all utilization of glucose, did not interfere so markedly with formation of ester phosphate. The rate of equilibration of cellular phosphate with labeled inorganic phosphate was only 20 per cent less than the control in the presence of a concentration of dinitrophenol sufficient to inhibit synthesis of cellular material completely.

To elucidate these results, experiments were designed to obtain information on the transfer of phosphate between the various organic phosphate fractions of the cells while enzyme or protein synthesis was occurring. It was necessary to label the various fractions of the cells before the experiment so that subsequent movement of phosphorus from one fraction to another could be followed.

Cells were grown in the usual medium in the presence of P^{32} labeled inorganic phosphate. The various fractions of cellular phosphate were all labeled in this way. After forty-eight hours, the cells were harvested, washed free of contaminating labeled inorganic phosphate by successive rinses with unlabeled $M/15$ KH_2PO_4 solution, and resuspended in a medium containing unlabeled $M/15$ KH_2PO_4 and 4 per cent glucose. The carbohydrate was fermented under completely anaerobic conditions. During the process of fermentation there was no budding or increase in protein nitrogen.

It was found that within four hours one-half of the total activity was lost from the cells. Practically all of this loss could be accounted for in the acid-soluble fraction, constituting about 50 per cent of the total cell phosphate. The acid-insoluble fraction (presumed mainly nucleoprotein) had lost no activity, in fact, it had gained slightly in both total (P^{31}) content and in labeled

cellular synthesis and growth. It is also suggestive that phosphate-transferring enzymes in general have been found particularly easy to inactivate with mustard gas and its nitrogen-containing analogues (12). As remarked before, these agents exert nucleotoxic effects remarkably similar to those found to result from x-ray and ultraviolet irradiation.

It would be premature to suggest that disturbances in nucleoprotein metabolism are the central factor in induction of the pathological manifestations observed to result from irradiation of cells. This discussion is already replete with analogies and speculations. There does appear to be sufficient evidence available to indicate that investigation of cellular responses to a wide variety of chemical agents may clarify many aspects of the radiation problem, particularly in conjunction with isotope studies. The direct extension of researches, such as those cited on phosphate transfer, to studies of cells under irradiation can be expected to yield data of fundamental importance in the elucidation of radiation effects.

Edward Mallinckrodt Institute of Radiology
510 S Kingshighway Blvd
St Louis 10 Mo

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DISCUSSION

(Papers by Quimby and McCune, page 201, and Kamen)

W Edward Chamberlain, M D (Philadelphia, Penna.) Dr Quimby always gives us a lesson in how to present a subject. I think probably everyone of you agrees with me in wishing that we could all present our material in such a clear, lucid way.

In a letter to me in advance of the meeting and in her remarks today, Dr Quimby said something about her paper not being very important. I disagree with her on that point. It is important. It is very important to have meticulous studies and measurements of this sort, and the fact that the outcome was as had been expected, that in certain hypothyroid children the thyroid uptake was what could be anticipated from the work of Dr Lawrence and Dr Hamilton and from Dr Quimby's own earlier work doesn't lessen its importance. It is impossible, of course, to discuss that paper because nothing remains to be said.

A totally dissimilar paper is that of Dr Kamen. It may be one of the most important papers that has ever been read at this Society, but I certainly feel that it is the kind of paper that we have to digest, that has to be read to be understood. In fact, Dr Kamen probably doesn't realize how ill-prepared we radiologists are for understanding his essay. He kindly sent me an advance copy and I have worked at it very hard. As a result of my study I advise you to read it when it is published and to study it.

Papers of this sort really should be read by title and, when published, should be accompanied by a glossary of terms and perhaps some remarks by a co-author to bring it down to our level. A very stimulating part of the paper to me was that it opened up a little window, showing us that perhaps such a study can be tied in with some exciting work presented at the Westinghouse Forum in May by some of the biophysicists and biochemists. All of a sudden one of them got up on the platform and said, "What is a virus?" A virus may be one of the smallest particles of matter that can reproduce itself and, if so—and there is some reason to think it is so—it may be the same thing as a gene. Now I noticed that Dr Kamen spoke of plasmagones and described them as those molecules that reproduce themselves inside of nuclei and then find their way into cytoplasm.

I think one statement he made may well be the key to something important in our study of cancer. Suppose these protein molecules, the smallest molecules that are able to reproduce themselves, should be poisoned by some injury to the body and should begin to reproduce themselves in altered form (maybe that is why cancer develops as a result of certain injuries). Tie this up with Dr Kamen's statement that these molecules are constantly reproducing themselves in large numbers in the nuclei and then finding their way into the cytoplasm, then recall the

the acid-soluble to the "nucleoprotein" fraction

When the cells were induced to synthesize new protein by the addition of ammonia or by forcing the adaptive synthesis of a new enzyme, the "nucleoprotein" fraction exhibited a different behavior. Typical experimental results are shown in Figure 2. In this experiment cells were

adapt to ferment maltose, *i.e.*, form a new enzyme, a similar drop in "nucleoprotein" P^{32} content was observed.

These findings can be summarized as follows:

1. Metabolizing cells which are not actively synthesizing new protein do not transfer phosphate from the "nucleoprotein" fraction.

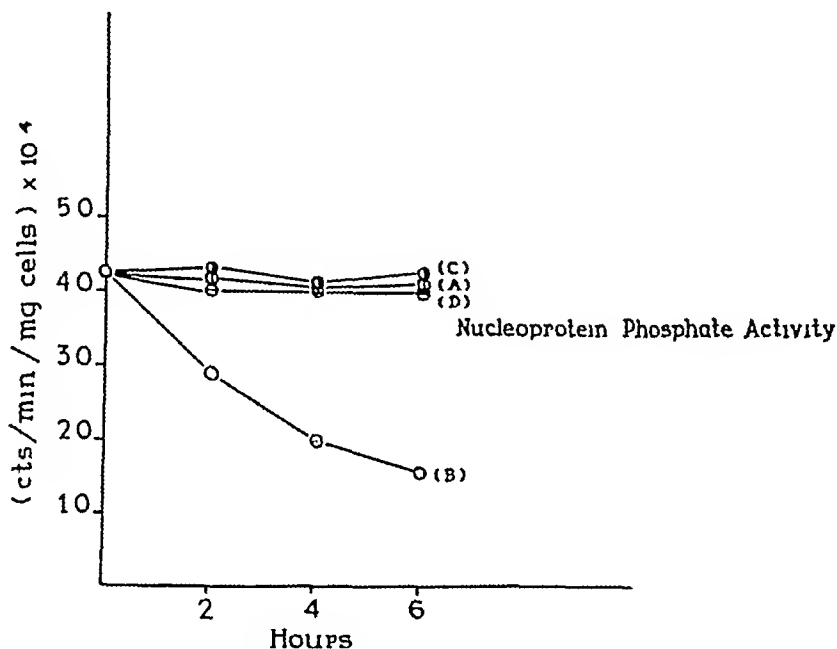


Fig. 2. Loss of phosphate from 'nucleoprotein' fraction as function of protein synthesis. Symbols explained in text.

suspended in four different media *i.e.*, (A) physiological saline and glucose, (B) physiological saline, glucose, and ammonium sulfate, (C) physiological saline, glucose, ammonium sulfate, and azide, (D) physiological saline, glucose, ammonium sulfate, and dinitrophenol. The concentrations of the azide and dinitrophenol were 5×10^{-3} and 5×10^{-4} M, respectively, so that enzyme synthesis was completely inhibited.

With glucose alone no change in P^{32} content was noted, whereas in the presence of ammonia the "nucleoprotein" P^{32} content fell to 38 per cent of its original value. It was found that both azide and dinitrophenol prevented this loss from the "nucleoprotein" fraction. When the cells were forced to

2. Synthesis of new protein or enzyme is associated with transfer of phosphate from the "nucleoprotein" fraction.

3. Agents which prevent enzyme formation and protein synthesis also stop flow of phosphate from the "nucleoprotein" fraction.

These results are in agreement with those of Caspersson in demonstrating a close connection between nucleic acid metabolism and protein synthesis. On the other hand, they extend those of Hevesy and his collaborators, since it is shown that not only the general turnover of phosphate but a continual supply of phosphate from nucleic acid is essential in maintaining

Hemangioendothelioma A Rare Malignant Tumor¹

VICTOR DRUCKER, M.D.²

New York, N. Y.

STOUT (10), Pack (6), and others have stated that hemangioendothelioma is a rare tumor. It is that belief that has led investigators to record their findings even in single cases (2, 3, 6, 7, 9) and has prompted the writer to offer the present report of an unusual example. The rarity of this tumor is substantiated by the fact that in the Department of Radiation Therapy at Bellevue Hospital, in a period of twenty-two years (1925-46), during which there were studied and treated many thousands of neoplasms, only 4 cases of hemangioendothelioma, pathologically confirmed, were observed. Through the courtesy of Dr. W. C. Von Glahn, director of the Department of Pathology, 4 additional cases were gathered from the various services of the hospital—an extremely low figure in view of the large number of surgical and pathological specimens seen yearly at this institution.

The unanimity of opinion that prevails as to the infrequency of this tumor does not exist, however, when the question of its malignant character arises. Sweitzer and Winer (11) consider hemangioendothelioma as an angiomatous tumor of low-grade malignancy. Schwartz (9) describes it as a malignant vascular tumor which may run a benign clinical course. Baumann-Schenker (1) is somewhat less optimistic, for, of the 5 cases reported by him, 2 proved fatal within fifteen months of treatment, 1 patient was alive with metastases to the base of the skull, and the other 2 were alive and free of clinical evidence of the disease (less than three years after treatment). Stout declares that, although the growth may be rapid or slow, its high degree of malignancy can be judged by the fact that of his series of 18

patients, 10 had died with metastases, 1 had local persistence of the disease, 3 had not been followed, and 4 were known to be alive. In only 1 of these last 4 cases, however, had more than five years elapsed after the excision of the tumor.

ETIOLOGY

Much speculation has arisen as to the etiology of hemangioendothelioma. Hewer and Kemp (7), reporting a case of hemangioendothelioma primary in the right auricle of the heart, with metastases to lungs, bronchial lymph nodes, mesentery, vertebrae, and skull, describe the concomitant finding of benign cavernous hemangiomas in the liver and esophagus. Since benign cavernous hemangiomas are usually multiple and widespread, the authors ponder the possibility that such a benign tumor might have been present originally in the heart wall and later undergone malignant change. Ogilvie and Mackenzie (8) press the premise that, as a group, tumors arising from vascular endothelium can be shown to run in a series of increasing malignancy, beginning with the congenital vascular nevus, proceeding to simple angioma, then to malignant angioma, finally ending in malignant hemangioendothelioma. Sweitzer and Winer quote Fraser as having postulated that hemangioendothelioma occurs as the result of the further evolution of a hemangioma which, after its formation, continues to grow by infiltration and active endothelial proliferation. Ewing (4) wrote that, in considering the "etiology of endothelioma, the influence of chronic irritation, trauma, and low-grade infection must be given a prominent place." Caro and Stubenrauch (2) report a case in which a hemangioendothelioma

¹ From the Department of Radiation Therapy, Dr. Ira I. Kaplan, Director, Bellevue Hospital, New York, N. Y. Accepted for publication in December 1946.

² Resident in Radiation Therapy, Department of Radiation Therapy, Bellevue Hospital.

possibility, suggested by someone else, that a virus may be the end result of a parasite which has lost all need for its cellular function except the function of reproduction, and finally consider the possibility that cancer is tied up with these reproducing molecules. I think you may see from this that a reading of Dr Kamen's paper when it is published will be exciting and stimulating and that it may be a new approach to a vital problem.

Edith H. Quimby, Sc.D. (closing) I want to thank Dr Chamberlain for his discussion, and I want to take issue with him on the subject of presenting fundamental scientific material in papers at our meetings.

I do not believe that such papers should be read by title. I think the essayist should make an attempt to recognize the limitations of a medical audience, and to a certain extent predigest the material for us, but I am afraid the radiologists in general will not read these articles in the journals unless they have been stimulated to do so. The best stimulation is a properly prepared report at a meeting, and I want to object strenuously to this audience being deprived of it.

However, I want to emphasize the matter of proper preparation. The essayist must consider his obligations to his audience and to his fellow speakers. The program has been prepared for a certain period, and each speaker knows his time allotment. His first duty is to prepare a version of his material which he can present within this time, and this does not mean a chopped-up version of the paper which is to be submitted for publication. It should mean a

carefully prepared digest of it. If this must include the defining of new terms, well and good, but there should not be a mass of scientific detail. The full account will be published for study, and it will be studied if the presented paper is properly stimulating. In this connection I recommend that everyone who presents a paper at a meeting should read the editorial published on this subject by Dr Golden in the *American Journal of Roentgenology* last April (1946).

Martin D. Kamen, Ph.D. (closing) I agree with Dr Quimby, except that if I had spent my time in defining terms I would have been through only half of the glossary in twenty minutes. I have written a much more extensive article than I gave you. I worked very hard at this paper and I hope people will read it. Indeed, I am very anxious to have people read it because I want to find out what is wrong with it. Incidentally, I entertained an unfortunate misconception of the time allowed for its presentation.

There is another thing to be said about the unfortunate chemist thrown into this melange. You will have to understand—and you will understand this quite clearly—that when you write an article for another group of people you are still aware that your own colleagues are looking at you and you cannot afford to be extremely labored about terms with which they are familiar. They will wonder why you are being so painfully clear. Usually in the hospitals they turn these articles over to biochemists or biologists to read. The result is that you may be looked at askance, and some of us are sensitive about that.

SUMARIO

Los Isotopos Radioactivos en el Estudio de los Efectos de la Radiación

Al discutir la aplicación de los isotopos radioactivos al estudio de los efectos de la radiación sobre las células, repásase también la labor de otros investigadores. El trabajo actual contiene el informe preliminar acerca de la naturaleza de los procesos químicos que intervienen en la síntesis de las encimas. Mediante el empleo del fósforo como localizador, se descubrió que (1) las células metabolizantes que no sintetizan activamente nueva proteína no transfieren fosfatos de la fracción "núcleoproteínica", (2) la síntesis de nueva proteína o encima se enlaza con la transferencia de fosfatos de la fracción "núcleoproteínica", (3) los agentes que impiden la

encimogenia y la síntesis de proteína también suspenden el paso de fosfatos de la fracción "núcleoproteínica".

Aunque sería prematuro indicar que los trastornos del metabolismo núcleoproteínico constituyen el factor central en la inducción de las manifestaciones patológicas derivadas de la irradiación de las células, parece que los datos disponibles y bastan para indicar que la investigación de las reacciones celulares a una amplia variedad de agentes químicos puede esclarecer muchas fases del problema de la radiación, en particular conjuntamente con los estudios de los isotopos.

tine, retroperitoneal space, ovary, uterus, corpora cavernosa, orbit, and central nervous system. The growth is not tender or painful. The cutaneous tumor is usually raised well above the surface, and the enveloping skin is normal until it is injured by trauma, at which time it will break down and there will be considerable bleeding, either outwardly from the surface of the tumor or inwardly into itself. Usually the tumor is soft and red. The rate of growth varies but is most often slow and progressive.

Metastases, which are common, occur through the blood stream, and sometimes through the lymphatics. Sites of metastatic involvement are the lungs, liver, spleen, pancreas, kidneys, adrenals, bones, skin, lymph nodes, diaphragm, and peritoneum. A feature of the tumor which has not been sufficiently stressed is a tendency to local recurrence after surgical removal. One of Stout's cases recurred eight times in nineteen years, and in one of Sweetzer and Winer's cases there were four recurrences in nine years.

The course of the disease varies. It can be a fulminating one, as in a case described by Stout in which the patient died eight weeks after first noticing the tumor in her breast, or it can be protracted, as in another case described by Stout, in which the patient had a tumor on the eyelid for twenty years.

Hemangioendothelioma cannot be definitely diagnosed clinically, since marked vascularity and hemorrhagic tendencies are not sufficient criteria for classifying a neoplasm as a malignant tumor of vascular elements. Histologic study is necessary.

Hemangioendothelioma has to be differentiated from hematoma, hemangioma, granuloma pyogenicum, malignant endothelioma, and Kaposi's disease (idiopathic multiple hemorrhagic sarcoma). A hematoma is present shortly after trauma, is usually tender, and histologically shows only blood clot. A hemangioma occurs in infancy or childhood, is generally flat, and histologically will show single layers of normal endothelial cells lining mature

vessels and dilated blood-filled capillaries. It must be remembered that hemangiomas are due to some impairment of the venous drainage mechanism in the involved area, resulting in stasis, engorgement, and dilatation of the vessels within the lesion, but without any inclination to malignant change. A malignant endothelioma shows a great predominance of cellular elements with little tendency to the formation of vessels. Granuloma pyogenicum shows no local infiltration, has a superficial purulent crust, and presents the usual polymorphonuclear response to inflammation. Kaposi's disease is characterized by bluish-red infiltrations which usually involve the lower extremities and, histologically, by blood vessel increase and dilatation, small hemorrhages with deposits of hemosiderin, and changes indicative of fibrosarcoma.

TREATMENT

According to Sweetzer and Winer, wide, thorough excision is enough to effect a cure of hemangioendothelioma but recurrence is possible. The recurrent tumor, fortunately, is as amenable to treatment as the original growth. The lesion is also responsive to irradiation, and Baumann-Schenker goes so far as to say that its radiosensitivity sometimes approaches that of the lymphoblastomata. Another method of treatment is a combination of surgery and immediate postoperative irradiation. Radiation therapy may be administered with x-rays or with radium. The choice will be determined by the accessibility of the lesion, its extent, and the type of modality available. Whether one uses superficial or high-voltage x-ray therapy will depend upon the thickness of the lesion and its location in the body.

A table showing the methods of treatment and results in the cases reported by Stout, Sweetzer and Winer, and the writer, is presented. Stout's series of 18 cases included 12 that had only surgical excision of the tumor, with local recurrences in 5, including the case previously mentioned with nine recurrences in twenty years.

TABLE I RESULTS OF TREATMENT OF HEMANGIOENDOTHELIOMA

Pro- cedure	Stout's Series			Sweitzer and Winer's Series			Author's Series		
	Number of Times Performed	Number of Recur rences	Died with Metastases	Number of Times Performed	Number of Recur rences	Died with Metastases	Number of Times Performed	Number of Recur rences	Died with Metastases
Surgery	21	12	6	8	6	0	2	0	1
Irradia- tion	0	0	0	1	1	0	0	0	0
Surgery + Irradia- tion	0	0	0	3	0	0	2	0	0

developed at the site of an injury, with wide invasion and a fatal outcome four months after the patient was first seen. Three of Sweitzer and Winer's patients gave a history of trauma, yet these writers declare that trauma cannot be considered as transforming a previously benign angioma into hemangioendothelioma.

PATHOLOGY

The term 'hemangioendothelioma' was first used by Mallory in 1908, to describe a malignant vascular tumor in which the endothelial cell is responsible for the aggressive growth and metastatic properties of the lesion. It has been described as a tumor made up of frequently anastomosing vascular tubes lined by atypical, hyperchromatic endothelial cells of varying size and shape which may form one layer or several layers, or may proliferate to such a degree as to obliterate completely the vascular tubes. The endothelial cells are generally within these tubes, but at times are found growing outside their confines in solid sheets. A delicate framework of reticulin fibers supports the vascular channels. The blood does not circulate through the tumor because of the immaturity of most of the vessels, although in the center there may be found some mature capillaries and larger vessels.

For malignant vascular tumors, as is true of so many other groups of tumors, there is, unfortunately, no generally accepted classification or terminology. Ewing listed hemangioendothelioma as "hemangioma hypertrophicum cutis" and defined it as "a slowly growing tumor of the skin or subcutaneous tissue occurring

chiefly in children, in which there is a nearly diffuse growth of endothelial cells with imperfect formation of capillaries." Geschickter (5) does not favor the term hemangioendothelioma, and the nearest thing to it in his classification is called a "metastasizing hemangioma," which is defined as "a superficial cellular angioma of the angioblastic variety which has been present as a benign growth for many years and which shows marked activity following trauma, and then metastasizes widely." Stout completely doubts the existence of "benign metastasizing hemangiomas." He studied the published reports of several such cases and, on re-examining the pathological specimens of the primary growths, found atypical endothelial cells as well as numerous anastomosing vascular tubes which convinced him that the tumors were hemangioendothelioma to begin with, and not simple benign hemangiomas.

CLINICAL FEATURES

Hemangioendothelioma may occur at any age, but more than half of the cases reported were in persons less than thirty years old. There is apparently no marked sex preponderance, of the cases collected by Stout, Sweitzer and Winer, and the writer, 15 were in males and 13 in females. The tumor varies in size from 0.5 cm. to 15 cm. or more in diameter (Fig. 1) and shows no predilection for any special part of the body, having been reported in the skin and subcutaneous tissues (2, 6, 10, 11), the breast (10), bones (3), tonsils, lungs, pleura, mediastinum, heart (7), pericardium, liver (8), spleen, lip, stomach, intes-

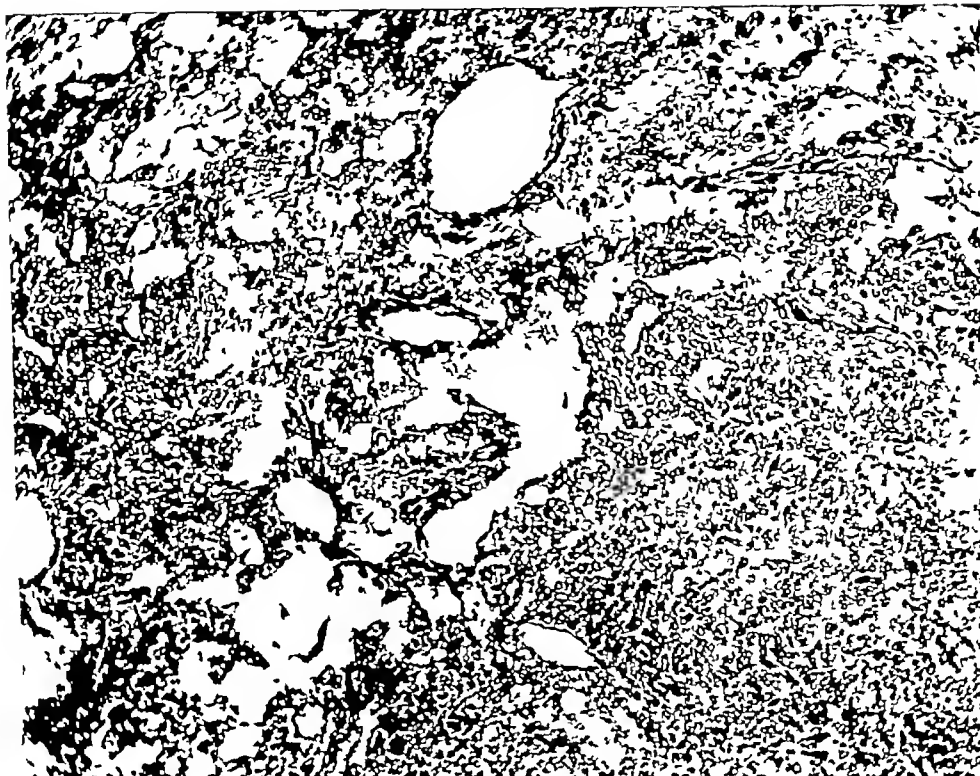


Fig 3 Photomicrograph of hemangioendothelioma showing malignant endothelial cells massed in solid sheets, in lower right field. Throughout the remainder of the field these cells are seen arranging themselves to form vascular channels ($\times c 130$)

was evacuated. There was profuse bleeding, and a pressure dressing was applied. On March 13, a mass as large as the original one had reformed at the operative site, and two days later it was again excised. More than "currant jelly" clot was expressed, and the ensuing hemorrhage was again checked by packing and pressure bandage. In neither instance was the blood clot sent to the laboratory for study. The patient was discharged on March 29, 1945.

On Nov 27, 1945, he was readmitted to the hospital because the mass in his cheek had recurred. It was now much larger than it had been on his previous admission and had been bleeding almost continually for the past three weeks. He stated that about four months after his discharge from the hospital, the tumor had begun to grow again. Two months later, a smaller growth arose from the lower portion of the large tumor and soon began to ooze blood.

Examination disclosed a large round mass, measuring 6 inches in diameter and elevated about 2 inches above the left cheek surface (Fig 1). The overlying skin was normal in color, tense, fluctuant and non tender. Springing from the posterolateral, dependent portion of the tumor was a smaller, spherical mass about 1 1/2 inches in diameter, which had an ulcerated granulating skin surface

that bled repeatedly (Fig 2). At this time, the patient appeared weak and chronically ill. Heart and lungs were normal, there was no hepatic or splenic enlargement, and no enlargement of the cervical, axillary, or inguinal lymph nodes. The blood count showed hemoglobin 7.5 gm, red blood cells 2,240,000, white blood cells 9,200 (72 per cent polymorphonuclear leukocytes, 26 per cent lymphocytes, and 2 per cent monocytes). Urinalysis was normal, and x-ray examination of the left facial bones showed no evidence of fracture. A biopsy specimen from the smaller mass, taken on Dec 6, 1945, was reported as an angiomatous tumor, but tissue from the deeper portions of the mass was requested for a better study.

On Dec 11, 1945, under intratracheal anesthesia, the external carotid artery was ligated, and the tumor was completely excised. It had to be resected from the parotid and submaxillary glands and the muscles of the cheek, down to the mucous membrane of the buccal cavity. In resecting it from the parotid gland, the nerve structures entering the gland, which included the facial, were divided. Five days later, left facial paralysis was evident, and ten days after the operation an external salivary fistula developed, which, however, closed spontaneously.

The histologic report on the surgical specimen described the tumor as composed mainly of broad



Fig 1 Illustrating the large size that a hemangioendothelioma can attain. Note that the dependent portion of the tumor has broken down and is oozing blood.

Fig 2 Demonstrating the smaller bleeding outgrowth from the dependent posterolateral region of the large hemangioendothelioma of the cheek.

Sweitzer and Winer's series of 6 cases included 4 treated by surgery only, with local recurrences in 3 (4 recurrences in a nine-year period in one). Irradiation combined with surgery in 3 instances resulted in no recurrences as late as twelve years after treatment though, oddly enough, 2 of the 3 patients had shown recurrences after previous treatment by surgery alone. In the writer's group of 4 cases, 2 had surgery only and the remaining 2 had irradiation after surgical excision. Of the former, 1 died with metastases and 1 was not traceable, the latter were alive one and a half and seven years, respectively, after treatment. Combining these figures, it is found that among 31 cases treated only by surgery, there were 18 local recurrences, while in 5 cases in which surgery was followed by irradiation there were no local recurrences.

REPORT OF CASE

A K, a white male aged 56, was admitted to Bellevue Hospital on March 5, 1945, in a semi-stuporous condition. He gave a confused story of having been struck on the head by another man and complained of a severe headache. His family history and past history were vague but apparently non-contributory.

There was a round, non tender, fluctuant mass in the patient's left cheek, as large as a baseball (3 inches in diameter). The overlying skin was not ecchymotic and there was no break in the buccal mucosa subjacent to the mass. Other findings were ecchymosis of both eyelids bilaterally, edema of the scalp, blood in the right nostril, bilateral spasticity, ankle clonus, and a positive Babinski reflex. Pulse, temperature, blood pressure, blood count, Wassermann reaction, and spinal tap were normal, but x-rays revealed a vertical fracture through the right frontal bone terminating in the inner region of the right orbit and extending backwards into the parietal bone. The left mandible showed no evidence of fracture. A diagnosis of fracture of the skull and hematoma of the left cheek was made.

On March 7, 1945 the mass in the left cheek was incised and about an ounce of currant-jelly clot

CONCLUSIONS

Most hemangioendotheliomata first come to the attention of the surgeon, and the method of attack is usually entirely at his discretion. Partly because most of these tumors are so readily accessible, and partly because they are not considered as highly malignant, simple surgical excision only is performed.

The summary in Table I shows that the best results are to be expected from surgical treatment in conjunction with radiation therapy. It is our firm belief that combined surgical and radiological treatment of hemangioendothelioma offers the hope of better control, and a more frequent cure, of a tumor which occasionally behaves like a benign growth but which more often takes on the character of a highly malignant process terminating in widespread metastases.

SUMMARY

(1) Hemangioendothelioma is a rare, slowly growing malignant tumor. Only 8 cases were seen and treated at Bellevue Hospital in twenty-two years.

(2) It is our opinion that the best treatment for this tumor is surgical excision followed by irradiation.

(3) An unusual case is reported.

NOTE: My thanks are tendered to Dr Rieva Rosh, Radiation Therapist at Bellevue Hospital, for her aid in the preparation of this paper, and to Dr W C Von Glahn, Director of the Department of Pathology, for his help in the collection and presentation of the pathological data.

786 Palisade Ave
Teaneck, N J

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SUMARIO

Hemangioendoteloma

En la mayor parte de los casos los hemangioendotelomas son primeramente observados por el cirujano a cuya discreción suele quedar por completo el método de tratamiento. En parte porque en la mayoría de esos tumores el acceso es fácil y en parte porque no se les considera muy malignos, el procedimiento habitual consiste en la simple excisión quirúrgica. El análisis de tres series de casos tomadas de la literatura revela, sin embargo, que se obtienen mejores resultados cuando la cirugía va seguida de la irradiación bien con los rayos X o el radio. Entre 31 casos tratados exclusivamente con la cirugía,

hubo 18 recurrencias locales y 7 muertes debidas a metástasis. Entre 5 casos que recibieron irradiación postoperatoria, no hubo recurrencias. Parece, por lo tanto, que la cirugía combinada con la radioterapia es el tratamiento de elección del hemangioendoteloma, ofreciendo un pronóstico más favorable en una forma de tumor que se comporta a veces como un tumor benigno, pero que más a menudo reviste la naturaleza de un proceso sumamente maligna, culminando en metástasis generalizadas. El caso descrito en este trabajo corrobora esta conclusión.



Fig 4 Appearance of patient after surgical removal of the mass. Note the extent of the scar and the classical signs of facial paralysis due to severance of the facial nerve

sheets of cells with large, pale, oval to round nuclei, and a moderate amount of light-staining eosinophilic cytoplasm. In several areas, these cells, typical of malignant endothelial cells, were seen to be forming moderate sized vascular channels, some of which contained red blood cells. A few mitotic figures were present. With Wilder stain the endothelial cells of the newly formed vascular tubes were shown to be enclosed by a fine framework of reticulin fibers. The diagnosis was hemangioendothelioma (Fig 3).

The patient was referred for postoperative radiation therapy on Jan 10, 1946. At this time further questioning brought out the startling fact that about a year before his first admission to the hospital he had noticed a small reddish 'sore' in the midportion of his left cheek. The 'sore' progressed slowly, at first but then began to grow more rapidly, just before he came into the hospital, it was about as large as a baseball as stated above. The tumor did not bleed, was not painful, and did not interfere with eating. There had not been any trauma to the face prior to the appearance of the sore.

Examination in the Radiation Therapy Clinic disclosed a long, vertical, healed scar on the left cheek, extending from near the external canthus of the eye, down over the mandible to the upper portion of the neck (Fig 4). The skin of the cheek in the region of the scar was hard and non-tender, the firmness extending through the cheek thickness.

There was no swelling of the face, but a typical left facial paralysis was present.

Deep x-ray therapy was administered directly over the scar 200 r (air dose) three times weekly, through an 8×10 -cm portal, carried to a total of 2,000 r. The technical factors were 200 kv., 20 ma., 50 cm skin-target distance, 0.5 mm Cu and 10 mm Al filtration, h v l 0.9 mm Cu.

When the patient was discharged from the clinic on Feb 4, there was a mild epidermitis of the cheek, no epithelitis, and no evidence of local recurrence. On re-examination in the clinic, on July 16, 1947, the skin showed no signs of radiation reaction and there was still no evidence of recurrence.

COMMENT ON CASE

Several interesting questions present themselves for consideration when this case is reviewed. To begin with, was the tumefaction of the cheek a hemangioendothelioma when the patient was first admitted to the hospital on March 5, 1945? Might this have been determined if the "clots" which were then expressed from the mass had been studied microscopically? If so, should not all extravascular blood clots removed from subcutaneous and deep tissues be studied histologically for possible evidence of vascular neoplasia?

Could the tumor in the cheek originally have been a hemangioma and have undergone a transformation into hemangioendothelioma as a result of the head trauma? Hemangiomas, however, are usually congenital, and manifest themselves long before the age of fifty-five, when this patient first noticed his lesion. There was x-ray evidence of a fracture on the right side of the skull with bleeding from the right nostril, but the tumor was on the left side of his head. The argument can be offered that there might have been a *contre coup* fracture—that the blow had been applied to the left side of the head and the force transmitted to the right side, but there was no ecchymosis and no other evidence of injury on the left cheek. It is highly improbable that this patient had had a hemangioma transformed by trauma into a hemangioendothelioma. The evidence does not favor such an inference.

² After this report was in the printer's hands

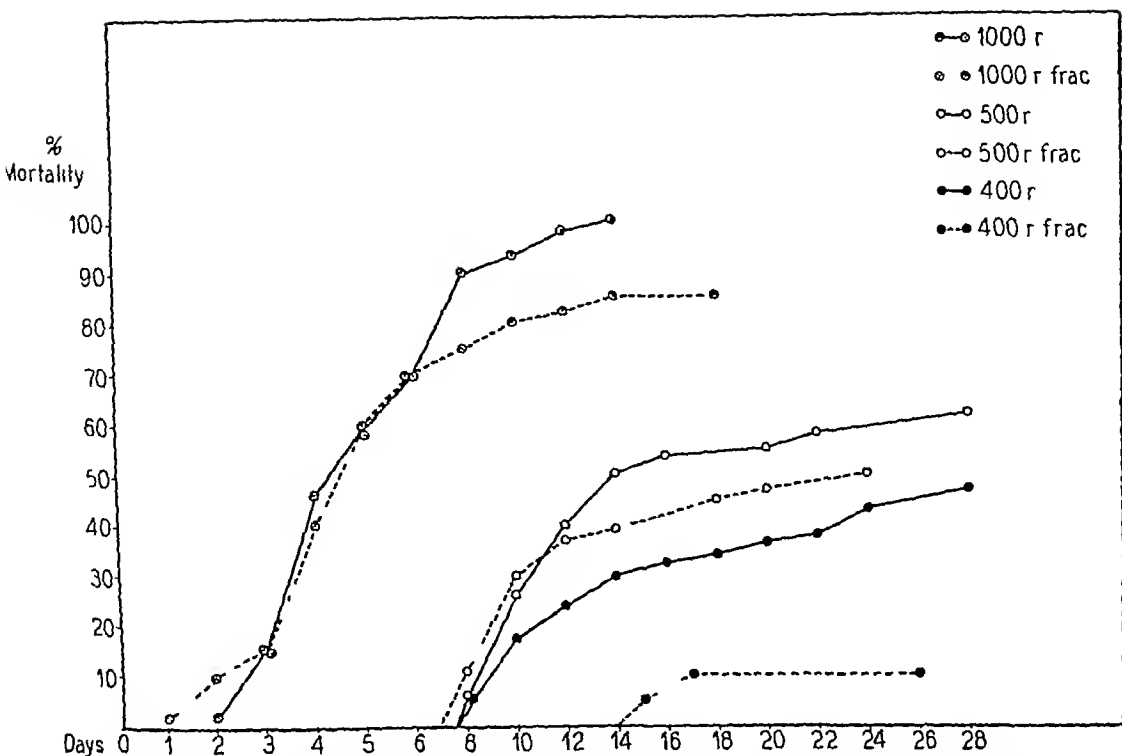


Fig 1 Mortality rates for mice receiving total body irradiation in single and fractionated doses

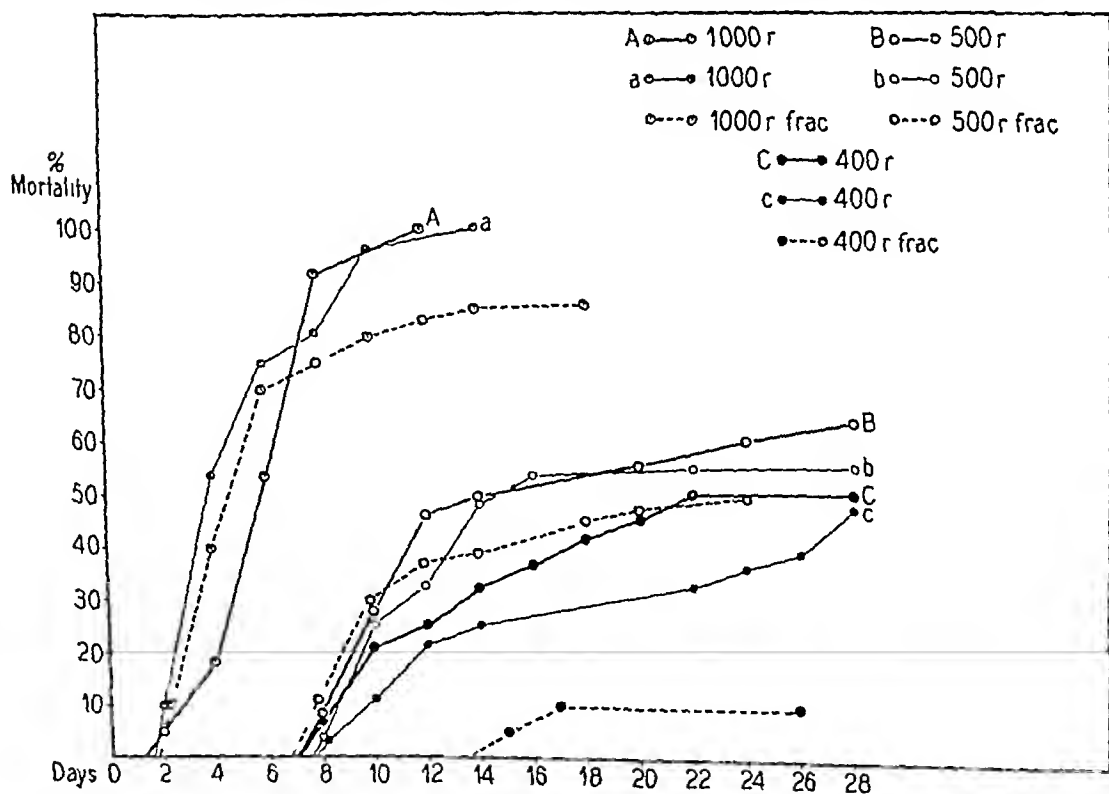


Fig 2 Mortality rates for mice receiving total body irradiation in single and fractionated doses. The mice receiving single doses are in each instance divided into two subgroups. See text.

Influence of Dose Fractionation on the Lethal X-Ray Effect Produced by Total Body Irradiation in Mice

A Preliminary Note¹

FRIEDRICH ELLINGER, M.D.²

IN PREVIOUS investigations it has been demonstrated that in various animal species increasing doses of x-rays in the form of total body irradiation produce an increasing mortality rate (1, 2). Data concerning the influence of dose fractionation on the lethal effect produced in mice by total body irradiation are presented in this paper.

The influence of dose fractionation on the biologic effect of x-rays has been the subject of a large number of investigations. From the accumulated evidence it appears that fractionation usually decreases the effect of a given dose administered in one exposure. In certain tissues and organs with high reproductive capacity, however, as, for example, the testis (3) and malignant tumor tissue (4), the effect of the fractionated dose was found to be more pronounced.

The mammalian body is composed of tissues known to react differently to dose fractionation. A study of its influence on the organism as a whole appears, therefore, of special interest.

METHODS

A total of 253 white male mice has been used in these experiments. The radiation factors employed were as follows: 200 kv p, 10 ma, 0.25 mm Cu and 1.0 mm Al inherent filtration, corresponding to a half-value layer of 0.75 mm Cu. The intensity of the radiation was 23.4 r/min. The distance from the target to the animal container was 50 cm, and the total field size 20 × 20 cm. The set-up for the exposures was the same as in our previous experiments (2).

Doses of 1,000, 500, and 400 r/air were given in one exposure and in fractions of 100 r/air on consecutive days (simple dose fractionation). These single exposure doses according to our previous experiences represent the LD 100, 50, and 35, respectively.

The choice of 100 r/air as the dose for each fraction of treatment was determined by previous experience, which showed that this dose represents the maximum effective dose, *i.e.*, the dose which in single exposure produces a marked effect within the irradiated body without causing fatalities.

Mortality rates for both groups, those receiving the radiation in a single exposure and those receiving the same total dose in equal installments, have been established by recording the number of fatalities daily. A graphic presentation of the results is made, as previously, by using the days after exposure as abscissa values and the percentage mortality as ordinate values. For correct comparison the graphs for the fractionated treated animals have been transformed in such a manner that the zero day in the fractionated group is the day on which the total dose in this group has been accomplished (*e.g.*, zero day for 500 r fractionated is the fourth day after beginning of treatment).

RESULTS

As shown in Figure 1, fractionation of each of the three investigated doses results in a decrease in the mortality rate.

The significance of these observations is illustrated in Figure 2. In this graph the lethal effect of the single exposure is presented in such a way that the total number

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² Research Associate in Radiology, Long Island College of Medicine.

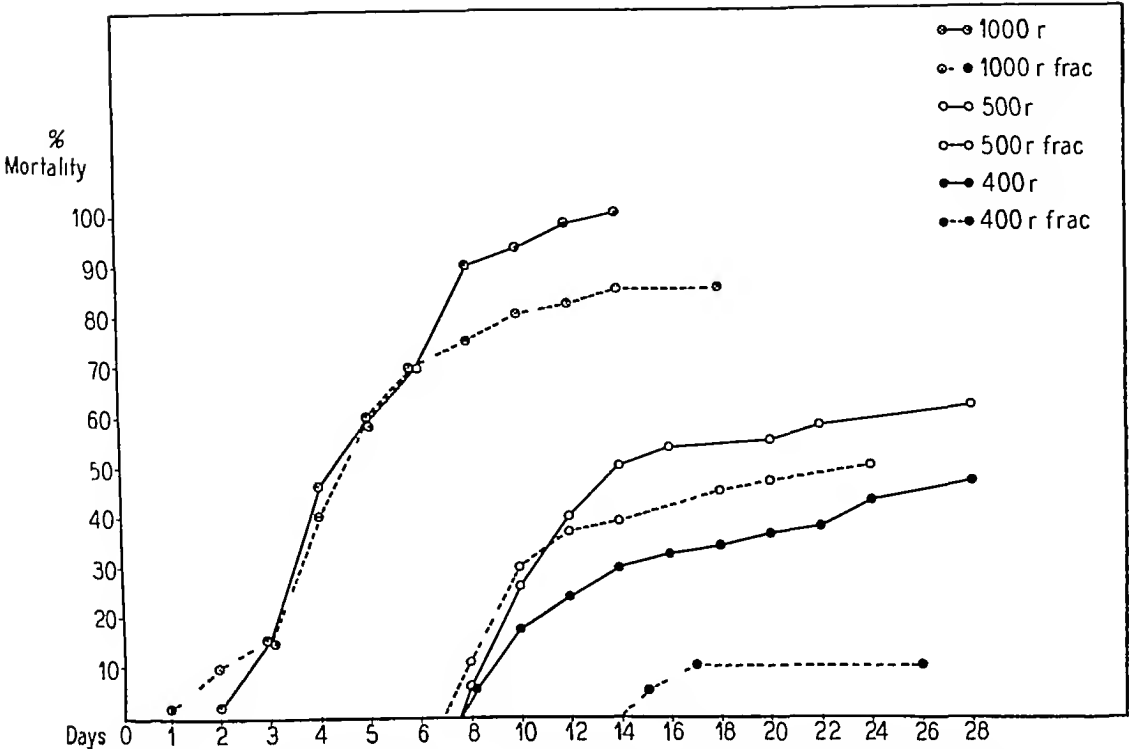


Fig 1 Mortality rates for mice receiving total body irradiation in single and fractionated doses

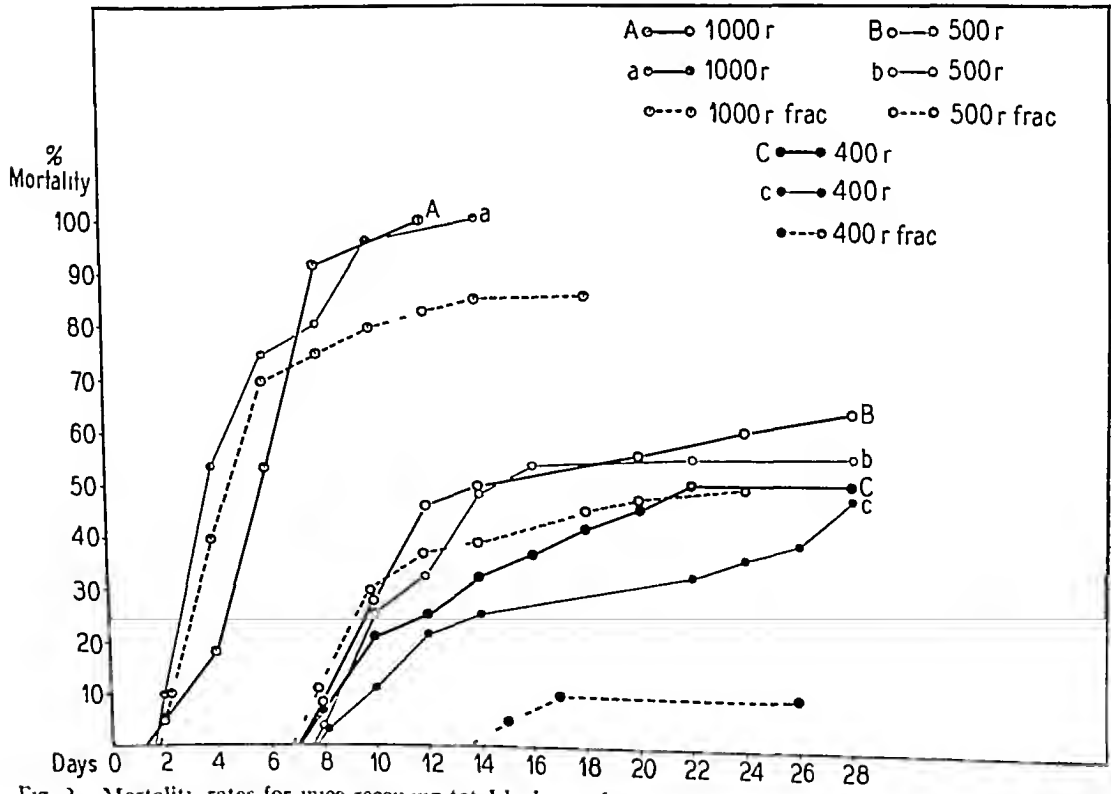


Fig 2 Mortality rates for mice receiving total body irradiation in single and fractionated doses. The mice receiving single doses are in each instance divided into two subgroups. See text.

of mice used for each dose has been divided into two groups and the mortality rate plotted for each subgroup (*A* and *a*, *B* and *b*, *C* and *c*). These two subgroups, permit appraisal of the consistency of the lethal effect for each of the three doses given in single exposure. As shown in Figure 2, in each instance the lethal effect of single exposure doses proved higher than that of the same dose fractionated.

The decrease in mortality rate in the mice receiving fractionated doses was accompanied by less pronounced changes in the general appearance of the animals. The fur appeared less ragged, and the loss in body weight in those animals which received 500 r was also less pronounced.

Autopsies of mice dying following fractionated treatment showed the same changes in the spleen and bone marrow and fatty changes in the livers previously described in those dying from the same doses given in a single exposure (2, 5).

DISCUSSION

It has been demonstrated that the lethal effect of certain x-ray doses given to mice as total body irradiation is decreased by simple fractionation. This phenomenon is most pronounced with the dose which produces the lowest mortality rate in a single exposure, as was to be expected.

Our data appear of particular interest in view of the recent studies by Henshaw (6) concerning the influence of fractionated irradiation on the life span of mice. Henshaw's interest was mainly focused on the determination of the tolerance dose in x-ray protection. His experimental approach, therefore, differed fundamentally from ours. He irradiated mice with minute daily doses of x-ray over the entire lifetime. The doses used ranged from 5 to 25 r/air, which doses in his experience, when given once, did not influence the white blood count. The exposures took place five times weekly. Even with the smallest dose of 5 r/air, amounting to as little as 1/200 of the absolute lethal dose (ALD) for mice, a definite shortening of the life span of the irradiated mice was

found. This indicates a definite dose accumulation under these very extreme conditions of fractionated treatment. These findings are of great importance in the problem of x-ray protection.

The interest of the radiation therapist in the problem of dose fractionation in total body irradiation is different. His clinical problem is whether or not a cancericidal dose of x-rays can be applied to the body as a whole without severe damage to the tumor host.

The demonstration that simple fractionation of lethal doses of x-rays decreases the mortality rate appears, therefore, of great significance. The fact that such a decrease has been accomplished by using single fractions amounting to as much as the maximal dose which can be given in a single exposure without producing fatalities seems particularly encouraging, as these doses are definitely effective on tumor tissue.

The data presented should be considered only as a qualitative result. They certainly do not permit any conclusions as to the amount by which fractionation decreases the effect in total body irradiation. They do, however, indicate the possibility of developing fractionated treatment schemata which will be far less dangerous to the host without impairment of the cancericidal action. The importance in the experimental radiation therapy of malignant tumors appears evident.

The proved consistency of the lethal effect of x-rays in mice is another interesting result of these investigations. This consistency is remarkable in view of the fact that these experiments have been conducted over a period of two years. Our data thus demonstrate the suitability of the lethal effect produced by total body irradiation of mice for quantitative studies of radiation effects.

SUMMARY

A comparison has been made between the mortality rates produced by various doses of x-rays given as total body irradiation to mice (*a*) in one exposure and (*b*)

in equal fractions on consecutive days simple dose fractionation) It has been demonstrated that simple dose fractionation decreases the mortality rates caused by the same doses when given in one exposure This decrease in mortality rate was found to be most pronounced with the dose which produced the lowest mortality rate in single exposure

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Long Island College of Medicine
Brooklyn 2, N Y

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SUMARIO

La Fraccionación y el Efecto Letal de los Rayos X

Comparados los coeficientes de mortalidad producidos por varias dosis de rayos X (1,000 r, 500 r y 400 r, en el aire) administradas a ratones en forma de irradiación total del cuerpo (a) en una exposición, y (b) fracciones iguales de 100 r en el aire en días consecutivos (fraccionación

simple de dosis), quedó demostrado que la fraccionación simple rebaja la mortalidad ocasionada por las mismas dosis administradas en una sesión Esta disminución de la mortalidad resultó ser más pronunciada con la dosis que produjo la mortalidad más baja en una sola sesión



EDITORIAL

Roentgen Therapy of Carcinoma of the Esophagus

That the radiation therapy of carcinoma of the esophagus presents us with one of our most difficult problems is universally recognized, more especially as no other form of treatment can claim equally good results from the standpoint of mortality or morbidity. The relative radioresistance of squamous-cell carcinoma and the usual extent of the growth before the occurrence of symptoms create a difficult primary problem, which is further complicated by the rather rapid involvement of the neighboring lymph nodes and the proximity of vital structures. To these difficulties are added the irritative effects of foods and fluids constantly passing over the involved area and eventual obstruction, leading to deterioration of the general health and inability to tolerate radical forms of therapy.

In assessing the results obtained from various types of therapy, consideration must be accorded the site of the tumor. Carcinomas involving the cervical portion of the esophagus are much more amenable to radiation therapy, since an adequate dose of radiation is more easily applied here, and the results are statistically better than for other esophageal cancers. In the thoracic portion, the esophagus is not only at a greater distance from the skin, making it more difficult to apply an adequate tumor dose, but it also lies in close proximity to vital organs whose presence gives the radiologist justifiable concern. Tumors in the region of the cardia are also relatively inaccessible, and their irradiation may involve considerable exposure of the liver, spleen, and stomach, resulting in leukopenia and other constitutional effects.

Radium therapy, extensively employed in the past for esophageal carcinoma, has been largely discontinued because of its

ineffectiveness and the untoward accidents which have attended it. The use of the radium bougie has given the best results, and a number of cases are recorded in the literature with survivals for varying numbers of years without evidence of recurrence of the original lesion. The disadvantages of the method are the local trauma, with imminent danger of perforation of the esophagus, and the high local dosage with rapid decrease of the depth dose, thus affording insufficient irradiation of adjacent lymph nodes.

Published series of carcinomas of the thoracic portion of the esophagus indicate that roentgen therapy is the most effective method of palliation, overcoming the obstruction with the least discomfort and danger to the patient. Uniform irradiation of the tumor and surrounding area is possible, and the danger of local trauma is eliminated. Even in this area the number of permanent cures is low. Excessive dosage may be delivered to the surrounding structures, as the lungs and the heart, and the tumor dose is therefore necessarily limited.

A careful study of 51 cases of carcinoma of the esophagus has been reported by Smithers, Clarkson, and Strong (3). Of the 51 cases referred for roentgen therapy, 44 were accepted and in 32 treatment was completed. In 5 of the 32 cases, the bulk of the tumor was in the upper third of the esophagus, in 21 in the middle third, and in 6 in the lower third. The radiation was given through six fields, 20×4 cm., at 400 kv, 80 cm focus-skin distance, with a half-value layer of 3.7 mm Cu. Six of the patients were living at the time of the report. One was alive and well four years after treatment, the others at various intervals, from thirteen to thirty-two

months Eight of the patients who died lived a year or more after treatment and one more than two years In 3 who died of metastases, all local symptoms had disappeared In no case was there evidence of fibrosis of the lungs, nor was there evidence of cardiac damage in any instance The skin effect was negligible, with only a mild erythema in most cases

In a small series of 5 cases, Buschke and Cantril (1) employed 800 kv, 100 cm target-skin distance, and 4.5 mm lead filtration One patient with involvement of the distal portion of the esophagus and the lesser curvature of the stomach was alive without radiological evidence of local recurrence after three and one-half years These authors believe that approximately 5,000 r must be delivered to the tumor and state that this is possible through one anterior and one posterior field

A series of 36 cases of cancer of the thoracic esophagus treated with medium-voltage roentgen therapy has been reported by Strandqvist (4) The factors used were 170-180 kv, target-skin distance 50 cm, filter 0.5 mm Cu plus 1.0 mm Al Strandqvist attempted to attain a tumor dose of 5,000 r over a period of forty days, but this goal was not always reached, even though six skin portals were used The skin and lung reactions were somewhat more annoying than in cases treated by others with higher voltage Injury to the heart due to direct irradiation of the cardiac region was observed in several cases This was a late complication and was not observed until six months to a year after treatment In this series of 36 cases there were 4 patients who lived two years or longer Of these, 2 were living and well at the time of the report Eighteen patients died within one year The author concludes that one cannot attain lasting cure without producing excessive damage to vital intrathoracic organs

From the Radium Center in Copenhagen, Nielsen (2) reports preliminary results of treatment of 174 cases of carcinoma of the esophagus by rotation therapy, at

180 kv with 0.5 mm Cu filtration The great majority of these—166, or 95 per cent—were situated entirely within the thoracic esophagus The patient is seated on a rotating stool and the position of the roentgen tube is fixed Fluoroscopy is used for centering the beam on the lesion and the rotation time is ten to fifteen minutes A tumor dose of about 5,000 r was given over a period of five to eight weeks The skin reaction was mild, consisting of a moderate dry epidermitis The general reaction was also slight, but there was usually a drop in the systolic blood pressure No final results are as yet available, but in 117 cases complete or nearly complete freedom from symptoms was obtained Contrasting the results with his previous results with cross-fire irradiation, Nielsen shows that 25 per cent of the patients as against 10 per cent in the former series were alive after one year Corresponding figures for two years were 15 and 4 per cent

It would seem from this brief review of the treatment of cancer of the esophagus that the results are much improved when voltages of 400 kv or more are employed for standard cross-fire irradiation A possible exception is the series treated by Nielsen with rotation therapy, though he believes that even better results would be obtained with supervoltage rays It is also noted that damage to the skin and even to the lungs and heart were less at the higher voltages The results appear to indicate that with supervoltage irradiation of carcinoma of the esophagus we may hope for a moderate number of cures, while relief will be obtained in a high percentage of cases

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EDITORIAL

Roentgen Therapy of Carcinoma of the Esophagus

That the radiation therapy of carcinoma of the esophagus presents us with one of our most difficult problems is universally recognized, more especially as no other form of treatment can claim equally good results from the standpoint of mortality or morbidity. The relative radioresistance of squamous-cell carcinoma and the usual extent of the growth before the occurrence of symptoms create a difficult primary problem, which is further complicated by the rather rapid involvement of the neighboring lymph nodes and the proximity of vital structures. To these difficulties are added the irritative effects of foods and fluids constantly passing over the involved area and eventual obstruction, leading to deterioration of the general health and inability to tolerate radical forms of therapy.

In assessing the results obtained from various types of therapy, consideration must be accorded the site of the tumor. Carcinomas involving the cervical portion of the esophagus are much more amenable to radiation therapy, since an adequate dose of radiation is more easily applied here, and the results are statistically better than for other esophageal cancers. In the thoracic portion, the esophagus is not only at a greater distance from the skin, making it more difficult to apply an adequate tumor dose, but it also lies in close proximity to vital organs whose presence gives the radiologist justifiable concern. Tumors in the region of the cardia are also relatively inaccessible, and their irradiation may involve considerable exposure of the liver, spleen, and stomach, resulting in leukopenia and other constitutional effects.

Radium therapy, extensively employed in the past for esophageal carcinoma, has been largely discontinued because of its

ineffectiveness and the untoward accidents which have attended it. The use of the radium bougie has given the best results, and a number of cases are recorded in the literature with survivals for varying numbers of years without evidence of recurrence of the original lesion. The disadvantages of the method are the local trauma, with imminent danger of perforation of the esophagus, and the high local dosage with rapid decrease of the depth dose, thus affording insufficient irradiation of adjacent lymph nodes.

Published series of carcinomas of the thoracic portion of the esophagus indicate that roentgen therapy is the most effective method of palliation, overcoming the obstruction with the least discomfort and danger to the patient. Uniform irradiation of the tumor and surrounding area is possible, and the danger of local trauma is eliminated. Even in this area the number of permanent cures is low. Excessive dosage may be delivered to the surrounding structures, as the lungs and the heart, and the tumor dose is therefore necessarily limited.

A careful study of 51 cases of carcinoma of the esophagus has been reported by Smithers, Clarkson, and Strong (3). Of the 51 cases referred for roentgen therapy, 44 were accepted and in 32 treatment was completed. In 5 of the 32 cases, the bulk of the tumor was in the upper third of the esophagus, in 21 in the middle third, and in 6 in the lower third. The radiation was given through six fields, 20×4 cm, at 400 kv, 80 cm focus-skin distance, with a half-value layer of 3.7 mm Cu. Six of the patients were living at the time of the report. One was alive and well four years after treatment, the others at various intervals, from thirteen to thirty-two



EBEN J CAREY, M D
1889-1947

ANNOUNCEMENTS AND BOOK REVIEWS

ALABAMA RADIOLOGICAL SOCIETY

At a recent meeting of the Alabama Radiological Society, the following officers were elected President, Dr John Day Peake of Mobile, Vice-President, Dr Lewis E Sorrell of Birmingham, Secretary-Treasurer, Dr Courtney S Stickley of Montgomery Dr Karl Kesmodel of Birmingham was nominated as candidate for Councilor to the American College of Radiology

RADIOLOGICAL SOCIETY OF NEW JERSEY

At a recent meeting of the Radiological Society of New Jersey, the following officers were elected President, Dr H R Brindle, of Asbury Park, Vice-President, Dr Wm H Seward, of Orange, Secretary, Dr Raphael Ponteranz, of Newark, Treasurer, Dr C A Plume, of Succasunna, Counselor, Dr Francis Carrigan, of Newark

NORTH CAROLINA RADIOLOGICAL SOCIETY

At a meeting of the North Carolina Radiological Society at Virginia Beach, on May 13, Dr C E Howard of Goldsboro was elected President for the ensuing year, Dr J P Rousseau of Winston-Salem, Vice-President, Dr James E Hemphill, Charlotte, Secretary-Treasurer

The meeting followed that of the Radiological Section of the North Carolina Medical Society under the chairmanship of Dr G W Murphy, of Asheville, in which the following speakers participated Dr Stuart Gibbs, Bowman Gray School of Medicine, Dr Robert J Reeves Professor of Radiology, Duke University School of Medicine, Dr Robert H Hackler, Washington, N C, Dr James E Hemphill, Charlotte, Dr C L Grav, High Point, Dr Allan Tuggle and Dr Thomas A Murrah, Charlotte Memorial Hospital

TENNESSEE RADIOLOGICAL SOCIETY

The Tennessee Radiological Society at its recent annual meeting elected the following officers for the coming year Dr J Cash King of Memphis President, Dr Franklin B Bogart of Chattanooga Vice-President, Dr J Marsh Frère of Chattanooga Secretary-Treasurer

Dr U V Portmann of Cleveland, Ohio addressed the Society on "Roentgen Therapy for Some Superficial Lesions" Dr Portmann was also guest speaker on the Tennessee State Medical Society program his subject being "The Role of Surgery and Radiation Therapy for Cancer of the Breast"

DR WARREN W FUREY HONORED

At its Annual Dinner on June 18 Dr Warren Furey took office as President of the Chicago Medical Society Members of the Radiological Society of North America, recognizing Dr Furey's invaluable services on their own behalf, congratulate their medical colleagues of Chicago on the wisdom of this choice

NATIONAL CANCER INSTITUTE

The resignation of Dr R R Spencer as Chief of the National Cancer Institute of the U S Public Health Service to be effective July 1 was announced at the last quarterly meeting of the Institute's National Advisory Council, in Bethesda Dr Spencer will, however, continue his valuable work in the field of cancer, devoting his full time to professional education and research His successor as head of the Institute is Dr Leonard A Scheele, formerly Assistant Chief Dr A C Ivy Vice President of the University of Illinois and one of the country's leading physiologists, becomes Executive Director of the National Cancer Advisory Council, succeeding Dr George M Smith who resigned some months ago for reasons of health

In Memoriam

EBEN J CAREY, M D

1889-1947

Eben J Carey, Dean and Professor of Anatomy in Marquette University School of Medicine, died of acute infectious hepatitis in Columbia Hospital, Milwaukee, on June 5, 1947, after a short illness While he was primarily an anatomist, Dr Carey was keenly interested in radiology and had been a member of the Radiological Society of North America since 1929

Eben J Carey was born in Chicago July 31, 1889, and acquired his preliminary education in California He then went to Creighton University Omaha, where he received the degrees of Master of Science and Doctor of Science and taught in the Department of Anatomy In 1920 he went to Marquette University as Professor of Anatomy Continuing his medical studies at Rush Medical School he received his M D from that institution in 1925 In 1934 he became Dean of the School of Medicine at Marquette

Dr Carey was nationally known as an anatomist, and many honors came to him His skill in the preparation of scientific exhibits was well recognized he served as Director of Medical Exhibits at the Cen

RADIOLOGICAL SOCIETIES SECRETARIES AND MEETING DATES

Editor's Note Secretaries of state and local radiological societies are requested to cooperate in keeping this section up-to-date by notifying the editor promptly of changes in officers and meeting dates Address Howard P Doub, M D , The Henry Ford Hospital, Detroit 2 Mich

UNITED STATES

RADIOLOGICAL SOCIETY OF NORTH AMERICA *Secretary-Treasurer* Donald S Childs, M D , 607 Medical Arts Bldg , Syracuse 2 N Y

AMERICAN RADIUM SOCIETY *Secretary*, Hugh F Hare, M D , 605 Commonwealth Ave , Boston 15 Mass

AMERICAN ROENTGEN RAY SOCIETY *Secretary* Harold Dabney Kerr, M D , Iowa City, Iowa

AMERICAN COLLEGE OF RADIOLOGY *Secretary* Mac F Cahal, 20 N Wacker Dr , Chicago 6 Ill

SECTION ON RADIOLOGY, A M A *Secretary*, U V Portmann, M D Cleveland Clinic Cleveland 6 Ohio

Alabama

ALABAMA RADIOLOGICAL SOCIETY *Secretary-Treasurer* Courtney S Stuckley M D Bell Bldg Montgomery Next meeting at the time and place of the Alabama State Medical Association meeting

Arkansas

ARKANSAS RADIOLOGICAL SOCIETY *Secretary*, Fred Hames, M.D., Pine Bluff Meets every three months and annually at meeting of State Medical Society

California

CALIFORNIA MEDICAL ASSOCIATION SECTION ON RADIOLOGY *Secretary* D R MacColl, M D , 2007 Wilshire Blvd , Los Angeles 5

LOS ANGELES COUNTY MEDICAL ASSOCIATION, RADIOLOGICAL SECTION *Secretary*, Moris Horwitz, M D , 2009 Wilshire Blvd , Los Angeles 5 Meets second Wednesday of each month at County Society Bldg

PACIFIC ROENTGEN SOCIETY *Secretary*, L Henry Garland M D 450 Sutter St , San Francisco 8 Meets annually with State Medical Association

SAN DIEGO ROENTGEN SOCIETY *Secretary*, R F Niehaus M D , 1831 Fourth Ave San Diego Meets first Wednesday of each month

X-RAY STUDY CLUB OF SAN FRANCISCO *Secretary* Ivan J Miller M D 2000 Van Ness Ave Meets monthly on the third Thursday at 7 45 P M , January to June at Lane Hall Stanford University Hospital and July to December at Toland Hall University of California Hospital

Colorado

DENVER RADIOLOGICAL CLUB *Secretary* Washington C Huyler M D , Mercy Hospital 1619 Milwaukee Deaver 6 Meets thurd Friday of each month at the Colorado School of Medicine and Hospitals

Connecticut

CONNECTICUT STATE MEDICAL SOCIETY SECTION ON RADIOLOGY *Secretary*, Robert M Lowman M D , Grace-New Haven Hospital, Grace Unit, New Haven Meetings bimonthly second Thursday

Florida

FLORIDA RADIOLOGICAL SOCIETY *Secretary-Treasurer* Maxey Dell Jr , M D 333 West Main St S Gainesville

Georgia

GEORGIA RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Robert Drane, M D , De Renne Apartments, Savannah Meets in November and at the annual meeting of State Medical Association

Illinois

CHICAGO ROENTGEN SOCIETY *Secretary*, T J Wachowski, M D , 310 Ellis Ave., Wheaton Meets at the Palmer House, second Thursday of October November, January, February March and April at 8 00 P M

ILLINOIS RADIOLOGICAL SOCIETY *Secretary-Treasurer* William DeHollander, M D St Johns' Hospital Springfield Meetings quarterly as announced

ILLINOIS STATE MEDICAL SOCIETY SECTION ON RADIOLOGY *Secretary*, Frank S Hussey M D 250 East Superior St , Chicago 11

Indiana

INDIANA ROENTGEN SOCIETY *Secretary-Treasurer*, J A Campbell M D , Indiana University Hospitals Indianapolis 7 Annual meeting in May

Iowa

IOWA X-RAY CLUB *Secretary*, Arthur W Erskine, M D , 326 Higley Building Cedar Rapids Meets during annual session of State Medical Society

Kentucky

KENTUCKY RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Sydney E Johnson, M D 101 W Chestnut St , Louisville

LOUISVILLE RADIOLOGICAL SOCIETY, *Secretary-Treasurer* Everett L Pirkey, Louisville General Hospital, Louisville 2 Meets second Friday of each month at Louisville General Hospital

Louisiana

LOUISIANA RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Johnson R Anderson, M D , No Louisiana Sanitarium, Shreveport Meets with State Medical Society

ture of Progress Exposition and from 1931 was Director of Medical Exhibits at the Museum of Science and Industry in Chicago

For his work on the x ray study of bone growth, Dr Carey was awarded the Gold Medal of the Radiological Society of North America in 1933. He was most sympathetic to the teaching of radiology to undergraduate students, and during his last school year he rearranged the teaching schedule so that time was available for the Department of Radiology to teach first-year students roentgen anatomy and to double the time given the junior class.

Eben Carey was a man of strong convictions and worked hard for the cause of organized medicine. He was a friendly man and a jovial companion. His presence at a meeting insured keen discussion and good fellowship.

Radiology has lost a strong proponent in his passing but medicine is richer because of his efforts.

S A MORTON, M D

DR ALBAN KOHLER

Word has been received of the death of Dr Alban Köhler of Wiesbaden, Germany. Dr Köhler was an Honorary Fellow of the American College of Radiology and was well known to American radiologists for his book on "Borderlands of the Normal and Early Pathological in the Roentgenogram," a work which has gone through many German and English editions. A letter from Dr Köhler, telling of the losses which he suffered in the war, appeared in *RADIOLOGY* for November 1946.

Book Reviews

ENGLISH-SPANISH CHEMICAL AND MEDICAL DICTIONARY, COMPRISING TERMS EMPLOYED IN MEDICINE, SURGERY, DENTISTRY, VETERINARY

BIOCHEMISTRY, BIOLOGY, PHARMACY, ALLIED SCIENCES AND RELATED SCIENTIFIC EQUIPMENT. By MORRIS GOLDBERG, Chief Technical Translator, Translation & Research Bureau, New York City. Author of *Spanish English Idioms*. A volume of 692 pages. Published by McGraw-Hill Book Company, Inc., New York 18 N Y. Price \$10.00.

An English-Spanish Chemical and Medical Dictionary should find a wide field of usefulness among chemists, physicians, laboratory workers, and others who are searching for Spanish equivalents to scientific terms in active English usage. According to the publishers more than 40,000 translations and definitions are included in this new dictionary by Morris Goldberg. Radiologists, however, will find that many words which are commonplace in their specialty are missing. Perhaps the most serious omission is the term *roentgen*, indicating the international unit of radiation dosage. Others, to select a few, are tomography, laminagraphy, grenz rays, cyclotron, betatron, isotope, phantom, diaphragm (Bucky), neutron, and proton.

The author makes a point of the fact that not only are Spanish equivalents of the English terms presented but that there are included, in addition, brief definitions in Spanish for correct and ready interpretation. This is an excellent idea, but in a work designed to cover so wide a field it has been impossible to extend these definitions beyond a few words, so that the general impression is one of oversimplification. It is assumed, however, that the book is designed for rapid reference rather than an intensive word study, in which case one should perhaps not be too critical.

The typography is excellent, and the general appearance of the book pleasing. It should constitute one more link in the bond of understanding between scientists of the Americas.



Pennsylvania

PENNSYLVANIA RADIOLOGICAL SOCIETY *Secretary*
Treasurer, James M. Converse, M D, 416 Pine
St., Williamsport 8 Meets annually

PHILADELPHIA ROENTGEN RAY SOCIETY *Secretary*,
Calvin L. Stewart, M D, Jefferson Hospital,
Philadelphia 7 Meets first Thursday of each
month at 8 00 P M, from October to May in
Thomson Hall, College of Physicians, 21 S 22d St

PITTSBURGH ROENTGEN SOCIETY *Secretary-Treasurer*,
Lester M. J. Freedman, M D, 415 Highland Bldg.,
Pittsburgh 6 Meets second Wednesday of each
month at 6 30 P M, October to May, inclusive

Rocky Mountain States

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY *Secretary-
Treasurer*, A. M. Popma, M D 220 N First St
Boise Idaho

South Carolina

SOUTH CAROLINA X-RAY SOCIETY *Secretary-Treasurer*,
Robert B. Taft, M D, 103 Rutledge Ave., Charles-
ton 16

Tennessee

MEMPHIS ROENTGEN CLUB Meetings second Tuesday
of each month at University Center

TENNESSEE RADIOLOGICAL SOCIETY *Secretary-Treasurer*
J. Marsh Frère, M D, 707 Walnut St., Chat-
tanooga Meets annually with State Medical
Society in April

Texas

DALLAS FORT WORTH ROENTGEN STUDY CLUB *Sec-
retary*, X. R. Hyde, M D, Medical Arts Bldg.,
Fort Worth 2 Meetings on third Monday of each
month in Dallas in the odd months and in Fort
Worth in the even months

TEXAS RADIOLOGICAL SOCIETY *Secretary Treasurer*,
R. P. O'Bannon, M D 650 Fifth Ave., Fort Worth
4

Utah

UTAH STATE RADIOLOGICAL SOCIETY *Secretary Treas-
urer*, M. Lowry Allen, M D, Judge Bldg., Salt
Lake City 1 Meets third Wednesday, January,
March May September, November

UNIVERSITY OF UTAH RADIOLOGICAL CONFERENCE
Secretary, Henry H. Lerner, M D Meets first and
third Thursdays, September to June inclusive
at Salt Lake County General Hospital

Virginia

VIRGINIA RADIOLOGICAL SOCIETY *Secretary* E. Latan
Flanagan, M D, 215 Medical Arts Bldg., Rich-
mond 19

Washington

WASHINGTON STATE RADIOLOGICAL SOCIETY *Sec-
retary-Treasurer*, Frederic E. Templeton, M D, 324
Cobb Bldg., Seattle 1 Meetings fourth Monday,
October through May, at College Club, Seattle

Wisconsin

MILWAUKEE ROENTGEN RAY SOCIETY *Secretary-
Treasurer*, C. A. H. Fortier, M D, 231 W. Wiscon-
sin Ave., Milwaukee 3 Meets monthly on second
Monday at the University Club

RADIOLOGICAL SECTION OF THE WISCONSIN STATE MED-
ICAL SOCIETY *Secretary*, S. R. Beatty, M D, 185
Hazel St., Oshkosh Two-day meeting in May
and one day at annual meeting of State Medical
Society in September

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE
Meets first and third Thursdays 4 to 5 P M, Sep-
tember to May, inclusive, Room 301, Service Mem-
orial Institute, 426 N. Charter St., Madison 6

CANADA

CANADIAN ASSOCIATION OF RADIOLOGISTS *Honorary
Secretary-Treasurer*, E. M. Crawford, M D, 2100
Marlowe Ave., Montreal 28, Quebec Meetings
in January and June

LA SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTROLOGIE
ET DE RADIOLOGIE MÉDICALES. *General Secretary*,
Origène Dufresne, M D Institut du Radium,
Montreal Meets on third Saturday of each
month

CUBA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA.
Offices in Hospital Mercedes, Havana Meets
monthly

MEXICO

SOCIEDAD MEXICANA DE RADIOLOGÍA Y FISIOTERAPIA
General Secretary, Dr. Dionisio Perez Cosío,
Marsella 11, México, D. F. Meetings first Monday
of each month



ORLEANS PARISH RADIOLOGICAL SOCIETY *Secretary*, Joseph V Schlosser, M D, Charity Hospital of Louisiana, New Orleans 13 Meets first Tuesday of each month

SHEVEPORT RADIOLOGICAL CLUB *Secretary*, Oscar O Jones, M D, 2622 Greenwood Road Meets monthly September to May, third Wednesday, 7 30 P M

Maryland

BALTIMORE CITY MEDICAL SOCIETY, RADIOLOGICAL SECTION *Secretary* Harry A Miller 2452 Eutan Place, Baltimore

Michigan

DETROIT X RAY AND RADIUM SOCIETY *Secretary Treasurer*, E R Witwer M D, Harper Hospital Detroit 1 Meetings first Thursday of each month from October to May at Wayne County Medical Society club rooms

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS *Secretary Treasurer*, R B MacDuff, M D, 220 Genesee Bank Building, Flint 3

Minnesota

MINNESOTA RADIOLOGICAL SOCIETY *Secretary*, C N Borman, M D, 802 Medical Arts Bldg, Minneapolis 2 Regular meetings in the Spring and Fall

Missouri

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY *Secretary*, John W Walker, M D, 306 E 12th St, Kansas City Mo Meetings last Friday of each month

ST LOUIS SOCIETY OF RADIOLOGISTS *Secretary* Edwin C Ernst M D, 100 Beaumont Medical Bldg Meets on fourth Wednesday of each month, October to May

Nebraska

NEBRASKA RADIOLOGICAL SOCIETY *Secretary Treasurer*, O A Neely, M D, 924 Sharp Building, Lincoln Meetings third Wednesday of each month at 8 P M in either Omaha or Lincoln

New England

NEW ENGLAND ROENTGEN RAY SOCIETY *Secretary-Treasurer*, George Levene M D, Massachusetts Memorial Hospitals, Boston, Mass Meets monthly on third Friday at Boston Medical Library

New Hampshire

NEW HAMPSHIRE ROENTGEN SOCIETY *Secretary-Treasurer* Albert C Johnston, M D, Elliot Community Hospital Keene Meetings quarterly in Concord

New Jersey

RADIOLOGICAL SOCIETY OF NEW JERSEY *Secretary* Raphael Pomeranz, M D, 31 Lincoln Park Newark 2 Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called

New York

ASSOCIATED RADIOLOGISTS OF NEW YORK, INC. *Secretary* William J Francis M D, East Rockaway L I

BROOKLYN ROENTGEN RAY SOCIETY *Secretary Treasurer*, Abraham H Levy, M D, 1304 Carroll St, Blyn 13 Meets fourth Tuesday of every month, October to April

BUFFALO RADIOLOGICAL SOCIETY *Secretary Treasurer*, Mario C Gian, M D, 610 Niagara St., Buffalo 1 Meetings second Monday evening each month, October to May, inclusive

CENTRAL NEW YORK ROENTGEN SOCIETY *Secretary-Treasurer*, Dwight V Needham, M D, 603 E Genesee St, Syracuse 10 Meetings in January May and October

LONG ISLAND RADIOLOGICAL SOCIETY *Secretary* Marcus Wiener, M D, 1430 48th St, Brooklyn 19 Meetings fourth Thursday evening each month at Kings County Medical Bldg

NEW YORK ROENTGEN SOCIETY *Secretary*, Wm Snow, M D, 941 Park Ave, New York, 28.

ROCHESTER ROENTGEN RAY SOCIETY *Secretary*, Murray P George, M D, 280 Crittenden Blvd, Rochester 7 Meets at Strong Memorial Hospital, third Monday September through May

North Carolina

RADIOLOGICAL SOCIETY OF NORTH CAROLINA *Secretary Treasurer*, James E Hemphill, M.D, Professional Bldg, Charlotte 2 Meets in May and October

North Dakota

NORTH DAKOTA RADIOLOGICAL SOCIETY *Secretary*, Charles Heilman, M D 1338 Second St, N, Fargo.

Ohio

OHIO RADIOLOGICAL SOCIETY *Secretary*, Henry Snow M D, 1061 Reibold Bldg Dayton 2 Next meeting at annual meeting of the Ohio State Medical Association

CENTRAL OHIO RADIOLOGICAL SOCIETY *Secretary*, Hugh A Baldwin, M D 347 E State St, Columbus

CLEVELAND RADIOLOGICAL SOCIETY *Secretary Treasurer*, George L Sackett M D, 10515 Carnegie Ave., Cleveland 6 Meetings at 8 30 P M on fourth Monday, October to April inclusive.

CINCINNATI RADIOLOGICAL SOCIETY *Secretary* Eugene L Saenger, M D 735 Doctors Bldg Cincinnati 2. Meets last Monday of the month September to May

Oklahoma

OKLAHOMA STATE RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Peter M Russo M D 230 Osler Building Oklahoma City Meetings three times a year

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height, and the cardiac phase and pulse rate. The posterior inferior boundaries of lungs and pleura in the living are likewise not in complete agreement with conventional anatomical teaching. According to the latter, the lungs and pleural cavities are separated posteriorly by a wide mediastinal space in which the esophagus is located directly in front of the spinal column. In contrast to this, roentgenograms occasionally depict the presence of a prevertebral space which is occupied by lung and pleura. The inferior pulmonary and pleural boundaries as shown roentgenographically are at a lower level than in anatomical preparations, and the pleural reflection frequently shows an upward concavity which has been wholly disregarded in textbook descriptions.

Lachman believes that as far as topographical anatomy is concerned, studies on cadavers should be replaced, wherever possible, by roentgenographic investigation in the living, which has already proved its value.

ELLWOOD W. GODFREY, M.D.

Solitary Pulmonary Tumor Cyst-Like Tumors Associated with Anomalies of Ribs Edgar Wayburn
Am Rev Tuberc 54 413-417 October-November 1946

The author reports 4 cases of a solitary, sharply circumscribed tumor found in U.S. Air Force personnel during a routine chest survey of 77,480 individuals. In each instance the lesion was small, measuring up to 3.5 cm in diameter and was located in the lower posterior right lung. In 3 of the cases there were associated rib anomalies (one patient had a cervical rib and the other two bifid anterior ends of the right fourth rib) which are believed to indicate the congenital nature of the pulmonary lesions. The opinion is expressed that they are bronchial cysts. Surgical exploration did not seem justifiable in view of the lack of symptoms and absence of disturbed function. The diagnosis, therefore, is only presumptive and no follow-up examinations are recorded.

L. W. PAUL, M.D.

Tuberculosis Survey Among Chinese Students R. Tak Eng
Am Rev Tuberc 54 385-388, October-November 1946

In a survey conducted during 1940 and 1941 before the Japanese occupation, a total of 5,234 students in private schools in Hong Kong were tuberculin tested. Of these 88.2 per cent showed a positive reaction. Even in the age group from six to ten 77.9 per cent reacted positively, above the age of 16 the percentage exceeded 90. Of the positive reactors 4,651 were examined fluoroscopically and 131 cases of tuberculosis were found (2.8 per cent). An additional 11 cases of pulmonary tuberculosis were found among teachers. Since tuberculous infection seems to be universal among the Chinese population in Hong Kong, the tuberculin test will be eliminated in future work, as only fluoroscopy and radiography are necessary for the detection of clinical tuberculosis.

L. W. PAUL, M.D.

Recurrent Spontaneous Emphysema of the Mediastinum with Concomitant Pneumothorax Report of a Case J. D. Schenck
New England J Med 235 511-513 Oct 3 1946

Spontaneous pneumothorax is important because of the possibility of injured ribs, coronary disease or myocardial infarct. It is quite possible that this con-

dition occurs more frequently than is generally recognized.

The author's patient, a 37-year-old white male, complained of a tight feeling in the lower chest, radiating along the left side of the neck. Previous experience of a chest pain had led to hospital admissions on various earlier occasions. The patient himself noticed a rhythmic noise within his chest that sounded like water dropping on a shelf. The noise was easily recognized by a visitor, and a physician heard it at a distance of about 5 or 6 feet. Examination at this time (December 1942) showed a pulse of 80 that was slightly irregular. The respirations, however, were normal, without dyspnea or cyanosis. Percussion of the chest showed an unusual degree of tympany over the cardiac area. Roentgenologic examination of the esophagus in various positions failed to reveal any evidence of an esophageal diverticulum or hernia.

The complaints subsided in a relatively short time, but in May 1943 the patient had another experience of dull pain in the cardiac and left infraclavicular areas again with audible rhythmic sounds heard at some distance from the chest. Several days later a complete examination showed some tympany over the cardiac region but the only laboratory finding beyond normal limits was a white blood count of 12,100. About two weeks after the onset of this episode a peculiar knocking sound could be heard with a stethoscope over the chest, apparently synchronous with some of the heart beats although skipping others. X-ray films of the chest at this time failed to reveal any evidence of air in the mediastinum but in oblique views a very small, marginal left-sided pneumothorax could be seen, which was quickly absorbed.

Discussing mediastinal emphysema, the author states that pain is the predominant feature although it may be entirely absent. It may radiate to the back, the neck, or to the left arm. Subcutaneous emphysema sometimes accompanies mediastinal emphysema. A frequent and important sign is the tympanic sound over the precordial area on percussion, however the most characteristic finding is the very audible sound of the heart beat even without a stethoscope at a considerable distance from the chest. Roentgenologically air may be demonstrated in the mediastinum, often best in an oblique position. Spontaneous mediastinal emphysema is believed to be due to air escaping from the bronchial tree and following the vascular trunks to the mediastinum, where it collects in large amounts. There is frequently an associated pneumothorax and when one condition is present a search should be made for the other.

JOHN B. McANENY, M.D.

THE DIGESTIVE SYSTEM

Diverticula of the Lower Thoracic Esophagus. Report of Six, Four of Which Were Operated Upon Robert M. Jones
Ann Surg 124 637-649, October 1946

Six cases of diverticula of the lower thoracic esophagus are reported. The condition is uncommon but should be considered as a possible cause of difficulty in swallowing and substernal distress. Diagnosis is based on the clinical history and barium studies of the esophagus. In 2 of the 6 cases, however, the condition was suspected from the plain roentgenogram. Preoperative and postoperative films are reproduced.

Diverticula responsible for symptoms and possibly

THE HEAD AND NECK

Porencephaly Eugene P. Pendergrass and Charles R. Perryman. *Am J Roentgenol* 56: 441-463, October 1946

The most widely accepted definition of porencephaly is that of LeCount and Semerkal who describe 'a defect communicating with the ventricles or separated from them by a thin layer of brain tissue, and covered on the outside by the arachnoid' (*Arch Neurol & Psychiat* 14: 365, 1925). This condition must be considered in the differential diagnosis of masses or contracting lesions involving the brain and since it is benign, its recognition is important in determining prognosis and therapy.

Porencephaly is broadly classified as developmental or acquired. Congenital vascular defects may cause porencephaly, while the significant acquired factors may be traumatic, vascular, or inflammatory.

Conventional roentgenograms may be negative, but more often some degree of asymmetry is evident. The most common finding is a change in the thickness of the skull on one side. It should be kept in mind that porencephaly is a manifestation of atrophy and may be the underlying lesion in hemiatrophy or underdevelopment. In such a case, the cranial vault on the affected side may be smaller, and there may be thickening or compensatory hypertrophy of the bones, elevation of the petrous ridge, and increased pneumatization of the petrous pyramid, mastoid, frontal and ethmoid sinuses. However, *encephalography or ventriculography is necessary to establish the diagnosis*.

In the 29 cases reviewed by the authors the condition is classified as "lobe," "interlobe" or "hemisphere" porencephaly according to the anatomical location and size of the lesion. Two thirds of the group had evidence of cortical or subcortical atrophy such as enlarged lateral ventricles or increase in the size of the subarachnoid pathways. A slight shift of the ventricles is usually present (88 per cent) more often toward the porencephalic side because of the accompanying atrophy. Reports are included of 3 cases which clinically and roentgenographically could not be distinguished from mass lesions.

ELLWOOD W. GODFREY, M.D.

War Injuries to the Mastoid and the Facial Nerve David Myers. *Arch Otolaryng* 44: 392-405, October 1946

Injury to the mastoid area and facial nerve is rare. Of a total of 4,400 battle casualties requiring surgical treatment at one military hospital only 12 were of this type.

Within the temporal bone are many vital structures in a small area so that the entrance of a foreign body may produce much damage. Often there are fractures of the dural plate or the lateral sinus plate and/or injury to the dura or lateral sinus. Blood, devitalized tissue, damaged bone and foreign bodies present ideal conditions for bacterial growth, and the combination of infection and injuries to important structures may lead to dangerous intracranial or systemic infection. Clinically few symptoms may be present to indicate the amount of damage and the real extent of the injury is

learned only at the operating table. There was purulent drainage from the middle ear and the mastoid area in all the patients in this series.

Roentgen studies are invaluable in injuries of the mastoid region. The examination requires detailed exposures of the area in at least two projections. It may be expected to reveal accurately the presence and location of foreign bodies, fractures and in most cases, infection. Fractures tend to be more extensive and in inflammatory changes more advanced than is apparent in the roentgenogram. Occasionally inflammatory changes are present in the mastoid cells when there is no x-ray evidence of infiltration.

The author believes that too much reliance is placed on chemotherapeutic agents, and that chemotherapy cannot take the place of surgical intervention nor compensate for incomplete surgical treatment in cases of the type under consideration. When an injury is localized to the mastoid a complete mastoidectomy should be done. If the middle ear is involved as well then a tympanomastoidectomy is indicated. A foreign body in the mastoid area also calls for mastoidectomy which makes it possible to ascertain the extent of the injury and remove both the foreign body and injured bone structures. This will result in rapid recovery. Otherwise a long period of disability may be anticipated with continued suppuration and the ever present threat of a dangerous complication. Injuries of the facial nerves present a special problem of diagnosis and treatment.

The 12 cases are presented in detail and a number of roentgenograms are reproduced.

THE CHEST

The Dynamic Concept of Thoracic Topography A Critical Review of Present Day Teaching of Visceral Anatomy. Ernest Lachman. *Am J Roentgenol* 56: 419-440, October 1946

The author enlarges and expounds the concept that the surface relationships of the thoracic viscera as determined in the cadaver differ in many respects from those in the living and cannot therefore serve as a proper norm for clinical purposes. The contents of the subdivisions of the mediastinum in the erect subject do not coincide completely with those found in the supine cadaver. According to anatomical teaching the bifurcation of the trachea is at the level of the intervertebral disk between the fourth and fifth thoracic vertebrae or at the level of the upper border of the fifth thoracic vertebra corresponding to the sternal angle between the manubrium and the body of the sternum. Roentgenography however reveals that in the upright adult subject it is usually considerably lower. It is highest in infancy and participates in the general descent of the viscera which takes place during the life span of the individual.

Many factors contribute to make the configuration of the heart extremely variable in the living. Foremost among these is the position of the diaphragm, which is influenced by respiration, body posture, the state of filling of the abdominal viscera, fat contents of the abdomen, etc. Other factors are the constitutional type of the individual, the age and sex, weight and

descending colon, sigmoid, and rectum. Considering the relative length of these different segments, the lesion is found six times as often in the right colon as in the transverse and four times as often as in the left colon.

The author stresses the importance of repeated x-ray studies. It has been his experience that a second or even a third examination may furnish information not at first demonstrated.

Two cases quite typical of the disease are reported. In one the lipoma was in the transverse colon and in the other in the descending colon. Both were removed by colotomy and local excision of the tumor with suturing of the bowel wall rather than by radical resection of the involved segment. The author believes that at operation the surgeon can usually differentiate these lesions as benign and so avoid resection, which carries a higher mortality.

BERNARD S. KALAYJIAN, M.D.

Roentgen Diagnosis of Volvulus of the Sigmoid with Intestinal Obstruction. Max Ritvo and J. Laurence. *Golden Am J Roentgenol* 56:480-488, October 1946.

Volvulus of the sigmoid is particularly likely to occur if the sigmoid is dilated long, and redundant. The authors mention chronic constipation, shortening of the mesentery, pressure from pelvic masses, and increased peristalsis as factors leading to such a condition. Clinically the patient may present a long antecedent history of abdominal pain and constipation. The acute attack is not infrequently preceded by some dietary indiscretion or the use of a purgative. The onset may be sudden and dramatic, and collapse and shock are not infrequent. Constipation is profound. Diarrhea with blood and mucus may be present. Cecostomy and intubation are of little help, and despite transfusions and infusions the patient's condition usually grows rapidly worse. In the past the mortality has been high—about 40 per cent—due largely to the difficulty of clinical diagnosis.

In the authors' experience the survey film of the abdomen will generally indicate low intestinal obstruction without definitely determining the site or nature of the obstruction. A barium enema administered under constant roentgenoscopic control is considered safe and provides invaluable data. Small amounts of barium are administered slowly and discontinued upon determination of the site and nature of the lesion. If the volvulus has produced complete obstruction the barium will fill only the ampulla of the rectum and lower sigmoid. At this point a rounded or tapered stenosis is noted, which is smooth in outline and sharply defined. When the obstruction is incomplete, small amounts of barium will pass through the narrowed lumen. Spiral linear densities alternating with narrow radiotranslucent bands over an area several centimeters in length delineate the torsion of the colon. This corkscrew arrangement of the mucosa is more satisfactorily shown on spot films made with pressure under fluoroscopic control, and is considered pathognomonic of volvulus. Further fluoroscopic examination, spot films and routine roentgenograms are made after evacuation of the barium.

Once the diagnosis is established surgery is indicated. Five cases of intestinal obstruction produced by volvulus of the sigmoid are included.

FLYWOOD W. GODFREY, M.D.

Diagnosis of Liver Abscess by Means of Thorotrast Hepatosplenography. Robert J. Reeves and Karl A. Youngstrom. *Texas State J Med* 42:310-314, September 1946.

The authors quote Ochsner's classification of the causative factors in liver abscess as follows: (1) transportation of virulent organisms through the portal vein from areas drained by the portal system (appendix, rectum, and other parts of the bowel), (2) extension from some contiguous disease process, as cholecystitis and cholangitis, gastric and duodenal ulceration and subphrenic space infection, (3) trauma, including penetrating injuries with introduction of microorganisms from without and subcutaneous injuries producing devitalization of liver tissue permitting growth of organisms already present in the liver, (4) blood borne infection with the production of metastatic abscesses, (5) amebic infection, which is the most common cause.

The possibility of peripheral development of abscesses is pointed out, and the accompanying signs are mentioned, such as diaphragmatic bulging and adhesions. [It is not mentioned, however, that in liver abscess there is more apt to be a blunting of the anterior costophrenic angle, whereas in subphrenic abscess arising from without the liver it is the posterior costophrenic angle that is more likely to be blunt.] Centrally located abscesses may be difficult to diagnose, and other lesions enter into consideration, as hepatomas, cholangiomas, cholangiohepatomas of both liver cell and duct elements, and tumors primary in the liver but not of specific hepatic elements (vascular, fibrous, adrenal rests, etc.).

It is in centrally located abscesses without liver enlargement that the use of thorium dioxide is particularly recommended. The senior author reported on this procedure as early as 1933, and in an experience of fourteen years has observed no significant damage from the medium. The average dose for injection is 75 c.c. colloidal thorium dioxide mixed with several hundred cubic centimeters of isotonic solution of sodium chloride. It is injected slowly over a thirty-minute period. The reaction, if any, is mild. In making the injection it is important to avoid infiltration in the subcutaneous tissues, as the thorium is absorbed and produces a hard painful mass. The presence of thorium is noted in the liver in several hours, and a roentgenogram taken a few hours after injection often shows sufficient contrast to outline a cavity or mass. The concentration in the reticulo-endothelial cells continues over several weeks, and the liver density increases. Since a liver abscess or tumor is devoid of active reticulo-endothelial cells, it will contain none of the thorium dioxide and will be of lesser density than the surrounding normal tissue. In this manner, the abscess may be easily demonstrated and accurately localized.

Three cases are reported and roentgenograms are reproduced.

SYDNEY F. THOMAS, M.D.

Biliary Calculi "Floating Between Two Fluid Levels": Employment of the Upright Position and Compression. Robert Coliez and Richard Hickel. *J de radiol et d'Electrol* 27:402-409, 1946.

The suggestion for the study recorded here came from several occasions upon which a gallbladder filled with dye was observed with the patient upright. The calculi were seen to float away from the fundus and to

all that may be described as giant diverticula, should be operated upon. In spite of the fact that only 1 of the 4 patients operated upon in this series could be considered a good operative risk, there was no death as a result of the procedure. Routine postoperative use of penicillin should decrease the danger of infection.

Pharyngo-Esophageal Diverticulum. Its Management and Complications. Frank H. Lalley. *Ann Surg* 124: 617-636, October 1946.

As the title implies, this paper deals chiefly with the surgical treatment of pharyngo-esophageal diverticulum. With regard to the roentgen diagnosis, the author states that a roentgenogram of a pulsion esophageal diverticulum is so distinctive that one would hardly think it possible to be mistaken as to its diagnosis, but such is not the case. In patients with a high web in the esophagus, in certain patients x-rayed postoperatively some time after removal of an esophageal diverticulum, and in others with high narrowing of the esophagus, there will be a dilatation with a spherical appearance roentgenologically which may lead the inexperienced observer to assume that what is really only a local dilatation is a true diverticulum. A true diverticulum is distinguished by the demonstration of its body, neck, and the spill-over into the esophagus of the thin barium mixture after the sac is filled. In most cases this spill-over appears in the lateral view as a thin line running from the neck down behind the sac. In those cases in which there is only a dilatation, if this thin line is visible it emerges from the bottom most dependent portion of the sac, where the narrowed point is, and in the lateral view will never be seen behind the suspected diverticulum.

Volvulus of the Stomach. Carl A. W. Zimmermann. *III South M J* 39: 782-786, October 1946.

The author reports in detail the case of a 71-year-old man presenting repeated vague attacks of indigestion. The attacks had occurred since childhood and appeared to be associated with fatigue or excitement. Among the complaints were epigastric fullness, pain, sensation as though food would not pass, followed by relief after noticeable food progress. Sometimes there was precordial oppression followed by belching.

Fluoroscopic examination showed the position of the stomach to be higher than normal. The rugal pattern was disturbed and peristalsis was not observed. The barium trickling through the pylorus. The course of the duodenum was directly downward. The patient was examined at a later date apparently during an acute attack. The uppermost portion of the stomach was the corpus which exhibited an air bubble outlining the greater curvature. The stomach was apparently rotated forward and upward on a horizontal axis.

Postmortem examination performed about ten years after the patient first came under observation showed an adhesion between the gastrocolic ligament and the left leaf of the diaphragm. The greater curvature in the extreme right border of the fundus was tipped anteriorly to a moderate degree.

This is the second case of volvulus of the stomach reported by Dr. Zimmermann. FRANCIS F. HART, M.D.

Duodenal Septum. Otis F. Lamson. *West J Surg* 54: 384-389, October 1946.

Duodenal septum is a rare congenital anomaly. Only 24 cases have been recorded and these in most in-

stances were found postmortem. The symptomatology is dependent upon the size and location of the opening in the septum. Even with a small opening symptoms are not likely to be observed until the child begins to take solid food. The opening may then become obstructed and a fatal termination may ensue. The picture is one of high intestinal obstruction similar to that due to other causes. Sometimes a flat abdominal film will reveal a gaseous dilatation of the duodenum.

Duodenal septum like atresia and diverticula is an embryological defect. Once it is discovered treatment consists in prompt removal.

The author reports a case in a woman of 28 with a history of "stomach trouble" since the age of two. The septum was discovered when the author performed a duodenojejunostomy for an enormously dilated duodenum. The opening in this case was laterally placed on the superior part of the septum which probably accounts for the patient's survival. The solid food which would have obstructed a central opening was held back and largely digested in the duodenum passing through the opening in liquid form.

MAURICE D. SACHS, M.D.

Chronic Ulcerative Colitis in a Girl. Agustín Castellanos and Raul Perciras. *Bol. Soc. cubana de pediat.* 17: 377-408, October 1945.

A case of chronic ulcerative colitis in a girl of nine and a half years with typical clinical, rectosigmoidoscopic, and roentgen findings is presented. The illness began when the patient was three years of age, and therefore at the time of the report was of almost seven years duration. Four roentgenograms of the colon taken in this period are reproduced. During the last three years the patient has shown a surprising improvement on sulfa medication. Various sulfa preparations (sulfanilamide, sulfathiazole, sulfapyridine, sulfasuxidine, sulfadiazine) have been tried during the periods of spontaneous relapse, but the majority of the time the patient has been on sulfaguanidine, most recently on talid sulfathiazole. The cultures were at first positive for the Sonne Duval dysentery bacillus, after two years of treatment twelve negative cultures were obtained.

The most surprising fact about this case is the necessity for giving sulfa medication daily to maintain normal stools. The effect is more evident with the insoluble preparations, especially with sulfaguanidine. Sulfasuxidine has shown the same antidiarrhetic action. Each time sulfa is suspended for two or three days, the diarrhea returns. The child has shown an extraordinary tolerance to this medication and during three consecutive years has taken around 2,200 grams of sulfa drugs without anemia, leukopenia, or toxic manifestations of any kind.

Submucous Lipoma of the Colon, with Report of Two Cases. F. G. Runyon. *New York State M J* 46: 2272-2275, Oct. 15, 1946.

Lipomas of the colon may be either submucous or subserous. The subserous variety rarely produces symptoms. The submucous type may be symptomless or may give rise to symptoms suggesting obstruction, intussusception, or a malignant growth.

In 109 of 121 lipomas of the colon recorded in the literature the location was satisfactorily determined: 46 per cent were in the cecum and ascending colon, 16 per cent in the transverse colon, and 38 per cent in the

descending colon, sigmoid, and rectum. Considering the relative length of these different segments, the lesion is found six times as often in the right colon as in the transverse and four times as often as in the left colon.

The author stresses the importance of repeated x-ray studies. It has been his experience that a second or even a third examination may furnish information not at first demonstrated.

Two cases quite typical of the disease are reported. In one the lipoma was in the transverse colon and in the other in the descending colon. Both were removed by colotomy and local excision of the tumor with suturing of the bowel wall rather than by radical resection of the involved segment. The author believes that at operation the surgeon can usually differentiate these lesions as benign and so avoid resection which carries a higher mortality.

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arrange themselves in a horizontal layer, separating the gallbladder shadow into two distinct parts. This observation led to experiments with gallbladders removed at operation, still filled with dye. The authors describe these studies and discuss the physical chemistry involved in stratum formation. The admixture of bile and dye is not a homogeneous one, which accounts for the derivation of two fluid levels.

With regard to the practical aspect of this phenomenon it is pointed out that compression such as is ordinarily used on the duodenal bulb enables one to visualize floating calculi when they might otherwise escape detection. The compression is applied with the patient upright.

The authors make the additional point that, in trying to establish a differential diagnosis between calculi and papillomata of the gallbladder, the fixation of the latter, demonstrable in this manner, may be of aid.

PERCY J. DELANO, M.D.

Artificial Pneumoperitoneum for the Diagnosis of Subdiaphragmatic Abscess. A. L. Wilkie and J. C. Clark. *Canad. M. A. J.* 55:200, September 1946.

In x-ray pictures made in the upright position after injection into the peritoneal cavity of 750 to 1,000 c.c. of oxygen, absence of a clear space between the liver and diaphragm (or on the left side, the stomach and diaphragm) is diagnostic of subdiaphragmatic abscess.

THE SPLEEN

Retropertoneal Splenomegaly: Occurrence in a Case of Leukopenic Plasma Cell Leukemia. Jack W. Bills and O. H. Perry Pepper. *Am. J. M. Sc.* 212:139-142, August 1946.

The spleen, as a result of a rare developmental anomaly, may occupy a wholly retropertoneal position. Such a condition may produce no symptoms but may be associated with a left hydronephrosis, perhaps due to the downward displacement of the kidney. The enlarged retropertoneal spleen, which lies posterior to the stomach and colon, also pushes the left dome of the diaphragm upward. It fails to present to palpation the characteristic splenic edges or notches.

A case is recorded in which the presence of an enlarged retropertoneal spleen complicated a leukopenic plasma-cell leukemia and added to the difficulty of diagnosis.

BENJAMIN COLEMAN, M.D.

THE MUSCULOSKELETAL SYSTEM

Paget's Disease: A Statistical Study of Eighty-Two Cases. Frank W. Newman. *J. Bone & Joint Surg.* 28:798-804, October 1946.

In this review of 82 cases of Paget's disease, the incidence was found to be equally distributed between the two sexes. The disease is one of late middle life, with extremes of twenty-one years and seventy years in the series recorded here. No familial tendency was apparent in any of the histories, although there was a history of diabetes in four of the families, but none of gigantism or hyperparathyroidism.

Only about half of the patients had complaints directly referable to the disease. These included pain in the bone or pain in the distribution of the cranial nerves. The remaining cases were discovered during examination for other reasons. The pelvis was most

frequently involved, with the skull second, followed by the spine and femur. Chemical studies showed the blood calcium and blood phosphorus levels to be within normal limits. Serum-phosphatase levels varied from 0.1 to 2.0 units, alkaline phosphatase levels from a low of 2.6 units to 48.8 units.

Roentgenographic examination was considered to offer the most characteristic findings. These were usually described as 'coarse trabeculations, osteoblastic lesions, osteolytic lesions, thickening of the cortex, new-bone production, bone destruction, cotton wool appearance, marked degenerative changes, and areas of increased and decreased density.' The possibility of metastatic carcinoma of the prostate had to be considered in many of these cases.

Complications usually encountered with Paget's disease were: (1) cranial nerve pressure, (2) fractures, (3) urinary calculi, and (4) sarcomatous degeneration. Cranial nerve pressure occurred in 26.8 per cent of the patients and usually involved the visual or auditory apparatus. Fractures occurred in 18.3 per cent, with union ensuing within a reasonable period of time. Urinary calculi were found in about 5 per cent of patients. Chondrosarcoma was observed twice.

X-ray therapy for Paget's disease has been practically abandoned. The most recent treatment consists in the administration of magnesium carbonate and a diet low in calcium.

JOHN B. MCANENY, M.D.

Secondary Myelofibrosis with Progressive Generalized Osseous Eburnation. S. R. Bersack and H. R. Feinstein. *Am. J. Roentgenol.* 56:470-479, October 1946.

Apart from primary myelofibrosis, fairly widespread fibrosis of bone marrow may occur in Paget's disease, myeloma, neoplastic osteal processes, bone metastases from prostatic carcinoma, septicemia, benzene and radiation poisoning, hyperparathyroidism, the various granulomatoses, and spent polycythemia. There are two prerequisite clinical elements: (a) destruction of a substantial portion of the blood-forming bone marrow and its replacement by a connective tissue derivative, (b) an attempt at compensatory hyperplasia by the remaining hemopoietic tissue. Such signs as weakness, bone pains, splenomegaly, and refractory anemia are directly predicated upon bone marrow replacement and the recruitment of all available resources for the production of blood constituents.

Both primary and secondary myelofibrosis may occur with and without osseous changes. According to Rosenthal and Erf (*Arch. Int. Med.* 71:793, 1943), about 50 per cent of the patients with myelofibrosis show on roentgen examination mottled rarefactions or irregular condensations in the cortical portions of the bones and splintering or elevations of the periosteum. Diffuse osteosclerosis is found in only a small percentage of cases.

The authors report a case of secondary myelofibrosis with progressive generalized osseous eburnation due to skeletal metastases from prostatic carcinoma. Only two similar cases are described in the English literature.

ELLWOOD W. GODFREY, M.D.

Bone Infarcts: Case Report with Autopsy Findings. S. C. Kahlstrom and D. B. Phemister. *Am. J. Path.* 22:947-953, September 1946.

This is an autopsy study of a previously reported case of bone infarction (*Am. J. Roentgenol.* 47:405, 1942).

Abst in Radiology 40 533 1943) which was diagnosed roentgenologically before death by the presence of blotchy medullary shadows of increased density produced by calcification of the unresolved portion of the infarcts. The authors believe that routine roentgenography of the bones of the extremities preceding autopsy would assist greatly in the recognition of old infarcts. A diligent routine search at postmortem examination would lead to the discovery of lesions in the early stages and help to arrive at the cause in those cases which remain unexplained.

Eosinophilic Granuloma of Bone, with Report of Case John T Bakody J Iowa M Soc 36 397-400, September 1946

A case of eosinophilic granuloma of the skull, diagnosed preoperatively, is presented. Treatment consisted of surgical excision followed by roentgen therapy (600 r). A tantalum prosthesis was fitted into the skull defect at the time of primary operation. The patient a 17-year old sailor subsequently returned to duty.

Labor Service and "Shovel Disease" E Wetzel Schweiz, med Wchnschr 76 990-991 Sept 28, 1946

The author reports a case of chip fracture of the spinous process of the first thoracic vertebra following exertion. These fractures induced by muscle pull are thought to be a hazard of heavy physical exertion and occur in the lower cervical or upper thoracic spine, especially in C7 or T1. There is no specific therapy.

LEWIS G JACOBS M D

Pathological Intervertebral Disk and Its Consequences. Contribution to the Cause and Treatment of Chronic Pain Low in the Back and to the Subject of Herniating Intervertebral Disk Olan R Hyndman Arch Surg 53 247-297 September 1946

The author distinguishes two entities, the degenerating intervertebral disk in which the nucleus pulposus and annulus fibrosus are undergoing disintegration but in which there is as yet no bulge or herniation to cause compression of nerve roots and the herniating disk in which a weakened capsule or annulus permits a bulge into the spinal canal. While these conditions are pathologically continuous the clinical syndromes produced are somewhat different even though they may coexist, which is the reason for this distinction. Patients in the first group usually give a history of chronic low back pain of years duration constantly localized in the lumbosacral region or the sacroiliac joint. There may be associated reflex pain down the posterior aspect of the thigh but this does not extend below the knee nor is it localized to the sciatic nerve. The pain occurs in periodic episodes usually associated with physical strain. The use of a soft mattress which promotes a flexed posture is also provocative of pain and there are usually stiffness and pain low in the back when an attempt is made to straighten up after having maintained a fixed posture. The pain is not exaggerated by coughing or sneezing. Physical examination is apt to be of little contributing value.

The herniated disk usually produces pain referred to the sacrum or lumbosacral joint and the sciatic notch radiating down the back of the thigh and leg or the lateral aspect of the leg to the calf, ankle or foot. This sciatic pain is present in the absence of low back pain in

about a quarter of the patients. While the pain is commonly unilateral, it may occasionally be bilateral. Remissions are characteristic but attacks are prone to become more frequent. Coughing and sneezing practically always aggravate the pain. Paresthesias are almost invariable. Contrary to observations in the presence of degenerating disks, lumbering up aggravates rather than relieves the pain. The straight leg-raising test produces pain on the affected side, circumferential measurement may show atrophy of the muscles, and hypalgesia of the sole of the foot and changes in the reflexes are often present. Occasional cases are seen in which an acute rupture of the nucleus pulposus occurs without antecedent disk degeneration and these are usually more acute and disabling in character.

Roentgen examination shows no characteristic signs on the plain film. While narrowing or collapse of a disk is suggestive it is not conclusive. When this is accompanied by hypertrophic changes on the posterior lip of the vertebra, however, herniation is always present usually of many years' duration. One of the principal values of this type of examination is to exclude tumor or other disease from the picture. It should be kept in mind that hypertrophic change which often accompanies this condition, may be confused with arthritis and an attempt to distinguish the conditions clinically is essential.

Pathological changes are discussed at considerable length. In summary the degenerating disk undergoes sequestration, the nucleus pulposus loses most of its water content and becomes fragmented and stringy. Its mucoid structure is replaced by fibrocartilage to some degree. There is however, no evidence of inflammation or necrosis. The annulus also degenerates and becomes thin eventually being unable to retain the sequestering nucleus. The etiology is not clear. The present consensus that trauma plays the important role is questioned. While maldevelopment is probably important it fails to explain the nature of the pathological changes.

Operation is recommended when the diagnosis of herniation is made. Myelography is usually unnecessary. The technique of operation and the postoperative care are discussed in detail. When proper attention is paid to the criteria for diagnosis the results are usually highly satisfactory. However in advanced cases with marked degenerative change, complete relief of symptoms is seldom obtained.

This treatise is a very superior discussion and will well repay reading in the original.

LEWIS G JACOBS M D

Value of the X-Ray Examination in the Diagnosis of Ruptured Intervertebral Disc. Harold O Peterson Minnesota Med 29 904 September 1946

The author points out the fact that the diagnosis of posteriorly herniated disk is not an easy one, that the most important feature of the diagnostic procedure is an examination by a clinician skilled in the approach to this entity, that roentgen signs may be misleading in themselves unsupported by adequate clinical confirmation.

This brief article is eminently sensible and comprehensive—the best the abstractor has ever read on the subject of herniated disk. It bespeaks not only an extensive experience in the handling of these patients but the faculty of excellent judgment on the part of the

essayist It is particularly recommended to those who have read and been impressed by the articles which ascribe diagnostic powers to air myelograms, projections of the spine in plain films followed by the measurement of minute intervertebral inequalities, or those who believe that intrathecal injection of opaque substances and speculative laminectomies may be casually undertaken

PERCY J. DELANO, M.D.

Bilateral and Multiple Ruptured Discs as One Cause of Persistent Symptoms Following Operation for a Herniated Disc Francis A. Echlin, Bertram Silverstone and Walter E. Scribner. *Surg., Gynec. & Obst.* 83: 485-493, October 1946

The authors believe that, in some cases at least, the recurrence or persistence of symptoms following removal of a herniated lumbar disk is due to the presence of bilateral or multiple herniations unrecognized at the original operation. They report a series of 60 cases in which operation was done for a suspected herniation of a lumbar disk. In 56 of these one or more herniated disks were found, in the remaining 4 both the operative and the myelographic findings were negative in spite of strong clinical evidence of herniation.

On the basis of the clinical observations, each of the 60 patients with 3 exceptions was believed to have a solitary unilateral herniated disk. Operation, however, showed 14 instances of bilateral or multiple herniations, 23.3 per cent of the 60 cases (6.6 per cent bilateral, 16.6 per cent multiple). Removal of the bilateral herniated disks required bilateral laminectomy.

Owing to the frequency of multiple herniations, the authors believe that myelographic studies with pantopaque are indicated in all cases prior to surgical intervention, although this procedure may be of little use in extreme lateral protrusions.

The authors add the opinion that the high incidence of multiple herniations in their series may be due to the fact that they were dealing with relatively severe cases. They also emphasize the point that operative relief of multiple disk herniation is not enough. Heavy work is particularly likely to precipitate postoperative symptoms in these cases.

The clinical, myelographic, and operative findings in some individual cases are discussed.

JOSEPH P. TOMSULA, M.D.

Complete Dislocations of the Acromioclavicular Joint. The Nature of the Traumatic Lesion and Effective Methods of Treatment, with an Analysis of Forty-One Cases. Marshall R. Urist. *J. Bone & Joint Surg.* 28: 813-837, October 1946

In this paper we have the largest collection of complete dislocations of the acromioclavicular joints reported by any one individual. The writer's impression of the great variation of the relationship of the acromion to the clavicle was confirmed by roentgen examination of 100 shoulders of unselected patients who had no complaint referable to the shoulder region. The study showed great variation in the form of the joint and indicated that there are relatively few acromioclavicular joints that correspond to the classical anatomical description. The findings are listed as follows: (1) The articular surface of the clavicle overrides the articular surface of the acromion. (2) The articular surfaces of the acromion and clavicle are nearly vertical and lie in the same plane. (3) The inferior margin of the articular

surface of the clavicle overrides the superior margin of the acromion. (4) The articular surfaces are incongruent, and the clavicle overrides the acromion. (5) The articular surfaces are incongruent, and are not in contact at any point. (6) The articular surfaces are incongruent, and the inferior margin of the clavicle overrides the superior margin of the acromion. These possible anatomical variations from the supposed normal joint structure may determine the success or failure of conservative treatment of acromioclavicular dislocations and the incidence of sequelae.

Much of this article is given over to details of treatment. Two observations of possible diagnostic and prognostic importance were noted in the course of the study, although the limited number of cases does not permit positive statements concerning them at this time. (a) An increase in the width of the joint space on the injured side, demonstrated roentgenographically, indicates posterior displacement of the outer end of the clavicle, even when the acromion process and the clavicle are correctly aligned. (b) Palpable posterior displacement and abnormal mobility of the outer end of the clavicle, after three weeks of healing, indicate the probable failure of conservative methods and the recurrence of the dislocation.

JOHN B. MCANENY, M.D.

Malignant Giant-Cell Tumor of the Bones of the Pelvis, Gluteal and Prostatic Regions N. Puente Duany. *Rev. med. cubana* 56: 678-688, September 1946

A case of giant-cell tumor invading the pelvic bones and the gluteal and periprostatic regions in a 43-year-old patient is reported. From a clinical point of view, it is outstanding because of the slow evolution (ten years) of the tumor and its invasive character, which resulted in the blocking of the lymphatic drainage and compression of the corresponding iliac vein and its tributaries, not usual in benign lesions. Anatomically, it differed from cases of malignant giant-cell tumor previously reported: first, it was diffuse; second, it affected at the same time the bones and soft tissues; and third, it did not metastasize to the lung. Roentgen therapy was given; 9,000 r were necessary to make the tumor disappear but produced a radionecrosis and ulceration.

Epiphyseal Coxa Valga. Report of Two Cases Alvis D. Finch and William M. Roberts. *J. Bone & Joint Surg.* 28: 869-872, October 1946

The usual residual deformity following slipping of the capital femoral epiphysis is a coxa vara. The possibility of a coxa valga has apparently been overlooked more or less, since no reports of this condition—at least in English—could be found. This report concerns two young Negro girls, both of whom had slipping of the capital femoral epiphysis with a resulting coxa valga rather than the usually seen vara deformity. Roentgenographic study of the pelvis showed the head of the femur to have slipped upward, laterally, and anteriorly in both patients.

The importance of recognizing this condition lies in the fact that reduction by forcible internal rotation is contraindicated, since this probably increases the deformity and may lead to a vascular necrosis of the epiphysis.

JOHN B. MCANENY, M.D.

Tibia Vara Louis Lamy and Léon Weissman *J de radiol et d'électrol* 27 409-414, 1946

The authors describe tibia vara as a special form of genu varum, the essential feature of which is a maldevelopment of the inner portion of the upper tibial epiphysis. The tibia angles inward sharply, but there is no real limitation of motion. Over 40 cases of this abnormality have appeared in the literature in the last twenty years.

In their discussion of the radiologic features of this condition, the authors include a number of illustrations. For those who cannot see these, it seems to the abstractor that the essential pathology can be clarified by comparing the developmental fault in these cases with a similar one seen at the lower end of the radius in a Madelung's deformity. In either case, one side of the epiphysis is much thinner than the other with a resultant articular tilting.

If one is interested in this entity he will find the authors' discussion of the pathogenesis well worth while, the literature is reviewed and various current theories as to remote etiologic factors are carefully weighed. Treatment is by osteotomy.

PERCY J DELANO M D

Para-Articular Ossification of the Soft Parts of the Ankle. Complication of Sprain With or Without Fracture of the Shaft of the Ipsilateral Fibula. Charles J Sutro *Arch Surg* 53 441-447 October 1946

The author reports 6 cases of sprained ankle in which protracted episodes of pain and swelling were accompanied by local para-articular ossifications. The patients were from eighteen to thirty-five years of age. They all experienced an unusually long convalescence, varying from four to seven months. In 2 patients a simple fracture of the fibular shaft accompanied by sprain led to a similar syndrome after removal of the immobilizing plaster-of-paris boots. On physical examination there were diffuse swelling and tenderness, ecchymosis and limitation of motion. Roentgen study demonstrated the presence of a small, thin vertical plaque in the region of the inferior transverse or posterior ligaments just posterior to the lower lip of the tibia. This tended to increase slowly in size and density but did not become attached to the bone. Treatment by reduction in the activity of the ankle, elastic support, and hydrotherapy produced symptomatic improvement but did not lead to absorption of the calcification.

LEWIS G JACOBS M D

Panner's Metatarsal Disease. A Condition of Aseptic Necrosis Simulating March Fracture. R C Van Demark and P V McCarthy *J Bone & Joint Surg* 28 842-844 October 1946

A 25 year-old male was suspected of having a march fracture of the left foot though x-ray films failed to reveal any change. Two months later a change at the distal end of the third metatarsal suggested peroneal reaction and march fracture was again suspected. Subsequent examination showed destructive and sclerotic changes which became more marked after an interval of two months. At that time definite cystic change was seen in the distal end of the third metatarsal. Examination ten months after the original complaint showed definite deformity of the metatarsal head.

Aseptic necrosis of the metatarsal is seen less often in the adult than in children. The possibility of the disease must be considered, however, and it must be differentiated from march fracture when the latter is a clinical possibility.

JOHN B McANENY, M D

Skeletal Lesions of the Foot from the Explosion of an Individual ("Antipersonnel") Mine. Le Gémisiel and R Sarrouy *J de radiol et d'électrol* 27 414-418 1946

The 'antipersonnel' mine described here is the German *Schumine 42*, consisting of a small plastic box containing some 200 gm of explosive, planted just below the surface of the ground, with a detonator which becomes effective with a weight of 20 to 25 kilos. The resulting explosion cripples the foot of the person stepping upon the mine, causing damage not approximated by anything seen in civilian life.

Roentgenograms showing typical injuries are reproduced. In general these followed two patterns depending upon whether the forefoot or the heel touched the detonator. In the anterior injury illustrated here, the metatarsals are extensively shattered and displaced, and the tibia is shattered at its lower end, the injury to the great toe is extensive. The fractures, the authors state, are frequently compound. In one case, the explosion virtually accomplished an amputation of the forefoot. In the posterior type, the force of the explosion is expended principally against the os calcis, with great damage and loss of substance. Curiously enough the talus is frequently intact, with extensive injuries above and below it. Some of the posterior injuries duplicate essentially a Chopart disarticulation.

The films illustrating this paper merit anyone's inspection. The abstractor has never seen in any type of foot injury anything to equal the shattering and comminution which characterize this *ped de mine*, or 'mine foot'.

PERCY J DELANO, M D

Sprain or Momentary Dislocation of the Talus? R Robert De Nicola *Occupational Med* 2 214-218 September 1946

A type of dislocation of the ankle which may easily be mistaken for a sprain is described. The unfortunate results from inadequate treatment are emphasized.

The serious fault of mistaking a momentary dislocation of the talus for a simple sprain may be avoided by performance of the "inversion test" graphically described by Watson-Jones in his book on *Fractures and Other Bone and Joint Injuries*. Subluxation of the talus is not a common injury, however, and the test is not recommended as a routine procedure in all injuries of the ankle. The test is indicated (1) when the routine lateral and anteroposterior roentgenograms show no bony injury but the force of injury is known to have been severe, signs of swelling, ecchymosis and tenderness are "excessive," a history of repeated sprains is obtained or the symptoms from the initial injury are delayed and (2) when routine films show some tilting of the talus, evidence of an old fracture of the ankle, evidence of traumatic arthritis or a bone spur on the astragalus.

Two cases of dislocation of the talus are presented and roentgenograms are shown for comparison with an inversion roentgenogram taken on a recently fractured ankle.

Calcaneo-Scaphoid Bar R K Magee and R A Benson *Canad M A J* 55 287, September 1946

This is a brief note describing an unusual anomaly demonstrated radiologically in a 37 year old soldier. It consisted in a congenital ossification in mesenchyme which would ordinarily form the lateral part of the short plantar ligament and was demonstrable in an oblique view as a solid bar of bone uniting the antero-internal angle of the calcaneus with the navicular.

THE GENITO-URINARY SYSTEM

Crossed Renal Ectopia. Haakon Odegaard *Acta radiol* 27 543-551, Aug 31 1946

The author presents the following theory as to the development of crossed renal ectopia. Under normal conditions the ureteral bud, which sprouts from the wolffian duct about the 25th day, has a transitory, dorsomedial direction of growth. When this ureteral bud continues to grow until it makes contact with the metanephrogenic tissue of the opposite side a crossed renal ectopia results.

The crossed ectopic kidney is in most cases hypoplastic. It lies below the other kidney and is often fused with it. The hilus usually is anterior to the kidney. The vascular supply, as a rule, is derived from vessels that supply the normal kidney. The ureter crosses the midline usually at about the 5th lumbar vertebra.

This anomaly is seen almost twice as frequently in men as in women. It must be differentiated from extreme degree of floating kidney, double or accessory kidney, displaced horseshoe kidney, and longitudinal ectopia.

The author presents 5 cases of crossed renal ectopia of which 4 were in men. In all the ectopic kidney was located distal to the normal kidney, three times on the left and twice on the right side.

PAUL W. ROMAN, M.D.

Spontaneous Rupture of the Kidney. Case Report. D E Beard *South M J* 39 780-782, October 1946

Beard adds a case of spontaneous rupture of the kidney to the 42 which he found previously recorded in the literature. In the reported cases predisposing causes were hydronephrosis, pyelonephritis, pyelonephrosis, tuberculosis, abscess, infarct, nephritis, tumor, aneurysm, and renal calculus. Parenchymal rupture is followed by sudden severe pain in the involved side, a rapidly appearing mass due to hemorrhage, and shock of varying degree. Two to three days later jaundice, general toxemia, and sepsis may appear. Symptoms and signs of pelvic tears vary depending on whether urinary extravasation is intra- or extraperitoneal. In the former event, sudden pain is followed by generalized peritonitis; in the latter a rapidly developing perinephritic abscess occurs. Excretory and retrograde pyelography are of diagnostic aid. Films may show extravasation of contrast media, deviation of the ureter around a hemorrhagic mass, obscuration of renal and psoas shadows, fixation of the kidney, and elevation of the diaphragm. The condition is considered a surgical emergency.

The author's patient was a 29-year-old colored laborer complaining of progressive dysuria and frequency for seven years. Cystoscopy revealed a grossly infected bladder of 30 cc capacity. A cystogram showed a

small contracted bladder, and excretory urography revealed a normal right upper urinary tract with failure of excretion on the left. Fifteen days after admission, while lying quietly in bed, the patient was seized with a sudden knife-like pain in the left upper quadrant which radiated posteriorly. Muscle rigidity and tenderness were marked. The patient was in mild shock. Within a few hours the temperature rose to 103° F, shock disappeared, and a hard, fixed, tender mass was palpable in the left kidney region. A left retrograde pyelogram showed a hydronephrotic kidney with a dense mass lying between it and the elevated diaphragm. Surgical exploration revealed a markedly enlarged left kidney with an intact but tightly distended true capsule. After 500 cc of purulent material was aspirated, a subcapsular nephrectomy was done. A small rupture measuring 1 X 1.5 cm was found at the superior pole, communicating with the superior calyx. *B. proteus* was cultured from the specimens. The patient received streptomycin postoperatively and made a satisfactory recovery.

WILLIS MANGES, M.D.

Roentgen Diagnosis of Diseases of the Neck of the Bladder. Athayde Pereira *Am J Roentgenol* 54 489-499, October 1946

Pereira considers urethrocytography necessary and even indispensable in the diagnosis of disease of the bladder neck. The following pathological conditions are discussed: valves of the neck, congenital atrophy of the neck, acquired atrophy of the neck, sclerosis of the neck, hypertonia of the sphincter of the neck, and hypertrophy of the trigonal muscle. The author describes his technique, the position of the patient, and the media used for urethrocytography. A brief discussion of accidents which may occur during urethrocytography, as well as contraindications to the procedure, is appended.

ELLWOOD W. GODFREY, M.D.

THE BLOOD VESSELS

Surgically Removed Foreign Body Embolus in the Pulmonary Artery. Solve Wehn, Carl Axel Hamberger, and Clarence Crafoord *J Thoracic Surg* 15 302-304, October 1946

A 21 year-old youth was struck in the groin by a flat sharp piece of steel which entered the femoral vein. The foreign body was never found in the leg, and over a year later when the patient was being examined for pneumonia it was seen in the lung at the left base. The past history was at first disregarded and the foreign body was thought to be in the bronchus but it was not demonstrable on bronchoscopy with fluoroscopic control and no bronchi were seen leading directly to it. The old history of injury in the leg was then correlated with the roentgenographic and bronchoscopic findings, and it was reasoned that the steel fragment entered the femoral vein and was carried thence to the heart and out into the pulmonary artery. On exploration of the lung the foreign body was after some difficulty located inside one of the pulmonary arteries. A small film was placed in a sterile glove and by holding this behind the suspected area a roentgenogram was made locating the foreign body. The vessel was then exposed and opened and the piece of steel removed. It measured 10 X 16 mm. There was no thrombotic occlusion of the vessel either before or after removal of the foreign body, and the patient recovered. This is believed to be the

first case in which a foreign body embolus was diagnosed reoperatively arteriotomy was done, the foreign body removed, and the vessel closed with a good result

HAROLD O. PETERSON, M D

Mediastinal Phlebography K Lindblom *Acta radiol* 27 521-525 Aug 31, 1946

The purpose of this paper is to call attention to the value of visualizing the mediastinal veins in the study of mediastinal tumors. The patient is placed in the left lateral position with a wool pad compressing the right jugular vein. Injection is made into the upraised right arm after venous stasis is produced in the left arm by a tourniquet. During inspiration 20 c.c. of diodrast are injected through a large needle into the right cubital vein within a period of one to two seconds. As soon as the injection is completed the exposure is made with horizontal rays. If necessary, the procedure may be repeated with the patient lying on the opposite side.

Two cases showed an aneurysm of the innominate artery bulging into the innominate veins. These were proved at autopsy. Two patients had malignant lymphomas of the anterior mediastinum. In one the tumor blocked the left subclavian, the jugular, the innominate and the caval veins. In the other, the left subclavian vein was blocked.

Five illustrations demonstrate the technic and show the findings in the cases studied.

S H MACHT, M D

TECHNIC

The Physicist in the Radiodiagnostic Department M H Jupe and L A W Kemp *Brit J Radiol* 19 301-313, August 1946

Jupe makes a plea for greater use of physicists in diagnostic radiology, pointing out that progress may be made in improved meters, testing meters and timers, control of incoming power, dark room procedures, better emulsions, body section radiography, and stereography.

Kemp reports a preliminary study of some of these problems in one department (at the London Hospital) with interesting results.

Tests of timer accuracy showed that an impulse timer had no error. Seconds timers showed errors of from 0 to 100 per cent. A device is described by means of which several timer tests may be made on one film.

There are many difficulties in determining the quality of a diagnostic beam. Preliminary studies showed that the second half-value-layer is more significant than the first. Tests upon two tubes showed a material difference in both quality and quantity. With modern types of line focus tubes there is a significant difference in both quantity and quality along an axis parallel to that of the tube. The intensity is materially less toward the anode end of the tube and the rays are harder, but the increase in hardness is not sufficient to make up for the decrease in intensity.

SYDNEY J HAWLEY, M D

Measurement and Calculation of Unsharpness Combinations in X-Ray Photography H A Klasens *Philips Research Reports* 1 241-249, 1945-46

The unsharpness with which a radiographic image is recorded is governed by three principal factors: (a) the unsharpness introduced by the finite size of the target of the roentgen tube (so-called geometrical unsharpness), (b) the unsharpness introduced by movement of the structure under examination (movement unsharpness), and (c) the unsharpness attributable to the characteristics of the screen with which the radiograph is made (screen unsharpness). Methods whereby geometrical unsharpness and movement unsharpness may be calculated for any particular condition are well known and are reviewed by the author. In the main, calculations derived by these methods coincide with observed impressions rather well for either one of these types of unsharpness alone. When the two types of unsharpness occur together, the observed unsharpness that results appears to be a complex function of the two unsharpness values. The complexity is further increased when screen unsharpness also enters the picture. Until recently methods of measuring and expressing screen unsharpness have not been satisfactory. The author, however, has developed a simple method in which the correlation between observed and calculated screen unsharpness values is extremely good. This same method has been expanded to permit the derivation of an expression by which the calculation of the total unsharpness which occurs when geometrical movement and screen unsharpnesses are present may be made. This expression may be written $u_o = (u_g^2 + u_m^2 + u_s^2)^{1/3}$ where u_o , u_g , u_m , and u_s represent the observed geometrical movement and screen unsharpnesses respectively. Calculations derived from this formula coincide closely with observed data.

RUSSELL H MORGAN, M D

RADIATION THERAPY

NEOPLASMS

Interstitial Irradiation Therapy in Carcinoma Originating at the Limbus: Report of Two Cases Treated With Radium Element Seeds L M Sykes *Texas State J Med* 42 376-379 October 1946

Two cases of squamous-cell carcinoma of the limbus are described with photographs before and after excision and the insertion of radium seeds (133 mg). In the discussion which follows it is pointed out that a small plaque can be used quite satisfactorily, furnishing a slightly larger source of radium with exposures as long as forty minutes. An ingenious method for fixation of the radium is described by Dr C M Griswold.

SYDNEY J HAWLEY, M D

Endolaryngeal Surgery Combined with Radiation in Late Laryngeal Cancer Millard F Arbuckle *Ann Otol Rhin & Laryng* 55 681-689 September 1946

This is a further report of the author's method of treating inoperable laryngeal cancer by roentgen irradiation following removal of the thyroid cartilage. An earlier paper by Arbuckle, Stutsman and Moore (*Ann Otol Rhin & Laryng* 53 689 1944) describing the procedure and presenting 18 cases has been abstracted quite fully in *RADIOLOGY* (45 316 1945).

Eight additional cases have now been treated. In none of these was the growth confined to the true vocal cord. The cancers were not as late, however, nor as widely distributed as those in the earlier series, and the patients were younger and healthier. There was one

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Beard adds a case of spontaneous rupture of the kidney to the 42 which he found previously recorded in the literature. In the reported cases, predisposing causes were hydronephrosis, pyelonephritis, pyelonephrosis, tuberculosis, abscess, infarct, nephritis, tumor, aneurysm and renal calculus. Parenchymal rupture is followed by sudden severe pain in the involved side, a rapidly appearing mass due to hemorrhage and shock of varying degree. Two to three days later jaundice, general toxemia and sepsis may appear. Symptoms and signs of pelvic tears vary depending on whether urinary extravasation is intra or extraperitoneal. In the former event, sudden pain is followed by generalized peritonitis, in the latter a rapidly developing perinephritic abscess occurs. Excretory and retrograde pyelography are of diagnostic aid. Films may show extravasation of contrast media, deviation of the ureter around a hemorrhagic mass, obscuration of renal and psoas shadows, fixation of the kidney, and elevation of the diaphragm. The condition is considered a surgical emergency.

The author's patient was a 29-year-old colored laborer complaining of progressive dysuria and frequency for seven years. Cystoscopy revealed a grossly infected bladder of 30 cc capacity. A cystogram showed a

small contracted bladder, and excretory urography revealed a normal right upper urinary tract with failure of excretion on the left. Fifteen days after admission, while lying quietly in bed, the patient was seized with a sudden knife-like pain in the left upper quadrant which radiated posteriorly. Muscle rigidity and tenderness were marked. The patient was in mild shock. Within a few hours the temperature rose to 103° F. Shock disappeared, and a hard, fixed, tender mass was palpable in the left kidney region. A left retrograde pyelogram showed a hydronephrotic kidney with a dense mass lying between it and the elevated diaphragm. Surgical exploration revealed a markedly enlarged left kidney with an intact but tightly distended true capsule. After 500 cc of purulent material was aspirated, a subcapsular nephrectomy was done. A small rupture measuring 1 X 1.5 cm was found at the superior pole, communicating with the superior calyx. *B. proteus* was cultured from the specimens. The patient received streptomycin postoperatively and made a satisfactory recovery.

WILLIS MANGES, M.D.

Roentgen Diagnosis of Diseases of the Neck of the Bladder Athayde Pereira *Am J Roentgenol* 56 489-499 October 1946

Pereira considers urethrocytography necessary and even indispensable in the diagnosis of disease of the bladder neck. The following pathological conditions are discussed: valves of the neck, congenital atrophy of the neck, acquired atrophy of the neck, sclerosis of the neck, hypertonia of the sphincter of the neck, and hypertrophy of the trigonal muscle. The author describes his technique, the position of the patient, and the media used for urethrocytography. A brief discussion of accidents which may occur during urethrocytography, as well as contraindications to the procedure, is appended.

ELLWOOD W. GODFREY, M.D.

THE BLOOD VESSELS

Surgically Removed Foreign Body Embolus in the Pulmonary Artery Solve Wehn, Carl Axel Hamberger and Clarence Crafoord *J Thoracic Surg* 15 302-307 October 1946

A 21-year-old youth was struck in the groin by a flat sharp piece of steel which entered the femoral vein. The foreign body was never found in the leg, and over a year later when the patient was being examined for pneumonia it was seen in the lung at the left base. The past history was at first disregarded and the foreign body was thought to be in the bronchus but it was not demonstrable on bronchoscopy with fluoroscopic control and no bronchi were seen leading directly to it. The old history of injury in the leg was then correlated with the roentgenographic and bronchoscopic findings, and it was reasoned that the steel fragment entered the femoral vein and was carried thence to the heart and out into the pulmonary artery. On exploration of the lung the foreign body was after some difficulty located inside one of the pulmonary arteries. A small film was placed in a sterile glove and by holding this behind the suspected area a roentgenogram was made locating the foreign body. The vessel was then exposed and opened and the piece of steel removed. It measured 10 X 16 mm. There was no thrombotic occlusion of the vessel either before or after removal of the foreign body and the patient recovered. This is believed to be the

The authors feel that the results with intravaginal rads were uniformly better in all groups, but particularly so in Stages II and III. In addition to the higher expectancy of life the group treated by vaginal cones enjoyed the advantage of fewer complications of treatment. These complications are detailed and analyzed. In conclusion the authors state that "in our experience the use of interstitial radon needles is relatively ineffective and dangerous as a method of controlling cervical cancer and we have abandoned it in favor of intravaginal and external roentgen therapy combined with intracervical radium."

ELLWOOD W. GODFREY, M.D.

Controversial Factors in the Management of Fundal Carcinoma. Lewis C. Scheffey, William J. Thudium, David M. Farrell, and George A. Hahn. *Am J Obst Gynec* 52: 529-540, October 1946.

The authors state at the outset that they are strong advocates of the advantages of irradiation in conjunction with surgery as a planned procedure in the treatment of fundal carcinoma. They then trace the steps which led them to this conclusion, reviewing their experience with 159 cases seen between 1921 and 1945. The length of the period covered makes possible the presentation of five year results for four different methods of treatment. One hundred and four patients were available for this record, which is as follows:

	Five year cures
1 Adequate surgery alone	62.5%
2 Radium therapy alone	45.8%
3 Radium therapy combined with external irradiation	36.6%
4 Adequate surgery with preliminary radium	90.0%

(There are 20 survivors in a more recent group of 21 patients who have been followed from one to four years.)

About 1930 the authors became impressed with the destructive action of radium upon endometrial carcinoma as observed in removed uteri and discouraged with roentgen irradiation because of its apparent ineffectiveness postoperatively and the occurrence, in some cases in which it was used prior to operation, of skin changes necessitating postponement of subsequent surgery. The procedure which eventually came into use and has been employed whenever possible since 1935 calls for 4,500 to 5,000 mg hrs of radium (screened with 1.5 mm of platinum) followed in six to eight weeks by complete hysterectomy with removal of the adnexa.

Whenever it is thought that endometrial cancer is deeply invasive or has passed beyond the confines of the uterus deep x-ray therapy is used to supplement the radium. The low survival rate in this group of patients, as given above, might be expected because the lesions were relatively far advanced.

It is felt that radium has a distinct advantage when used preoperatively not only because it causes local cancer destruction (residual carcinoma often attenuated) but because it may devitalize the growth even at some distance from the radium. RUSSELL WICH, M.D.

Wilms' Tumor. A Review of Sixteen Cases. Reed M. Nesbitt and Frederick M. Adams. *J. Pediatr* 29: 297-303, September 1946.

A series of 16 cases of histologically proved Wilms' tumor in children, treated at the University of Michigan Hospital during a nine year period, is presented. Three of the cases did not entirely conform with the usual pathologic picture but are included in the series because they were indistinguishable clinically from a typical Wilms' tumor. Two of these cases were diagnosed as adenocarcinomas, one of which might have been a variant of a Wilms' tumor, the third was diagnosed as a teratoma.

The diagnosis of a Wilms' tumor is not difficult. In a child, usually under five years of age, with a history of progressive abdominal enlargement and a firm, nontender smooth or finely nodular mass which usually fills half the abdomen, one can quickly make a presumptive diagnosis. The second most common abdominal tumor in childhood and the one which gives the most difficulty in differential diagnosis, is the sympathoblastoma, or neuroblastoma, of the adrenal. Diagnosis is usually established by pyelography. Subcutaneous or intravenous injection of diodrast is quite simple and in many instances satisfactory results are obtained. Retrograde pyelography is restricted almost entirely to females and those cases in which the other two methods are unsuccessful. The so-called characteristic pyelographic changes seen in a Wilms' tumor are: (1) distortion of the renal pelvis and calices, (2) displacement of the renal pelvis upward, downward or laterally, depending on the position of the tumor within the kidney, and (3) failure of visualization of the kidney pelvis. When no contrast medium can be seen in the pelvis or calices on the affected side the diagnostician must think of hydronephrosis as well as neoplasm. Aspiration as a diagnostic procedure has been thrown into discard.

The following policy has been adopted for treating these patients. Preoperative irradiation is reserved for those cases in which the tumor is so large that operative removal presents serious technical difficulties. This naturally means that the majority of the patients receive preoperative irradiation for one of the outstanding features of this tumor is the enormous size to which it grows before giving rise to any symptoms. Postoperative irradiation was formerly employed only in those patients in whom regional metastases were grossly evident at the time of operation or pathologic study of the regional lymph nodes showed metastatic involvement. Now however, all patients are given postoperative irradiation and the authors feel that 3 of the 8 living patients very definitely owe their survival to irradiation.

Of the 16 children in this series, 8 are still living for a period ranging from three and one half to eleven and one half years since the institution of treatment. One child, considered inoperable because of questionable chest metastases, was treated by x-ray alone. She has survived ten years and today appears well. Twelve of the 16 patients had nephrectomies and 7 of these children have lived long enough postoperatively to be considered cures by the standards set up by most authors. Two of these patients at operation had gross evidence of retroperitoneal extension of the tumor. They were given postoperative irradiation and the fact that they are still living shows adequately the value of this procedure. With one exception all of the 5 patients who had nephrectomies and have since died showed evidence of metastases within six months postoperatively. In the one exception three and one half years intervened before recurrence of the tumor was evident. Operation

death in the series. One patient was still under treatment at the time of the report, and the remainder were well, without evidence of cancer.

The diagnoses (clinical and microscopic) in the 8 cases were: epidermoid carcinoma (grade not given) in 2, epidermoid carcinoma, grade II, in 1, epidermoid carcinoma, grade III, in 2, carcinoma with metastases to lymph nodes and perichondrium (no grading) in 1, squamous-cell carcinoma, grade I, well differentiated, in 1, squamous-cell carcinoma, grade III, in 1. Prior to 1940 laryngectomy would have been recommended in all of these cases. Though the author states that for the cure of cancer larger doses of radiation are necessary than are commonly used even to the point of burns of the skin and extreme irritation of the mucosa, excessive amounts were not employed in this group—1,800 to 2,000 r to either side of the neck, which is less than in the Coutard fractionated technic.

Since the longest period that has elapsed in any of the cases treated by this method (including the earlier series) is six years, the author does not attempt to prophesy the future results either as to permanent cure or late radiation reactions. He has had no operative deaths and none due to irradiation. Total laryngeal stenosis had not occurred. One patient had a high degree of stenosis due to loss of the cricoid cartilage, but his voice was still usable. STEPHEN N. TAGER, M.D.

Comments on a Case of Lymphosarcoma of the Tonsil Which Did Not Respond to Roentgen Therapy
Miguel Guerrero Noyer. *Rev. med. cubana* 56: 30-37, January 1945.

A case of tumor of the tonsil and left lateral wall of the pharynx in a 7-year old boy is presented. The tumor had developed over a six months period. A diagnosis of lymphosarcoma was based not only on the type of lymphoid cells of which the tumor was composed but also on its fibrillary stroma and the widespread presence of macrophages. The tumor failed to respond to roentgen therapy (6,000 r), and the patient died three weeks following operation.

Bronchiogenic Carcinoma. Gustaf E. Lindskog. *Ann. Surg.* 124: 667-672, October 1946.

A series of 100 unselected cases of primary bronchiogenic carcinoma is analyzed. In 65 cases the growth was considered hopelessly advanced and inoperable when the patient was first admitted. Thirty-eight of these patients received only symptomatic care. Three patients refused treatment. Twenty-nine received high-voltage roentgen therapy, radon implantation or both. All of these are dead, the shortest period of survival (after admission) being two months and the longest thirty-three. The average duration of life in this group was 7.4 months, an increase of doubtful significance over the untreated cases. However, in the treated group there was very significant palliation in the form of relief of pain, decrease of dyspnea, improved aeration and bronchial drainage, as well as psychotherapeutic benefit.

Surgical exploration was carried out in 32 cases. No positive tissue diagnosis was available in 20 of these patients despite various diagnostic studies. In 20 of the 32 cases a non-resectable tumor was found. Nine of these patients had no subsequent roentgen irradiation and the average life span was eight months; 11 patients receiving roentgen therapy lived an average of 11.8 months. This difference is not statistically significant. Twelve patients were submitted to surgical resection

(10 pneumonectomy, 2 lobectomy), with a hospital mortality of 25 per cent. Three patients (2 pneumonectomy, 1 lobectomy) had survived 2.5, 4.0, and 5.0 years and were clinically well at the time of the report, all had squamous-cell carcinoma.

One patient, with anaplastic carcinoma in the mediastinum, is living and working three and one-half years after roentgen irradiation. He is the only patient in whom roentgen therapy produced a strikingly lasting effect.

Cancer of the Cervix. Study of the Effect ofInterstitial Radon Needles as Compared with Roentgen Therapy Given through Intravaginal Cones. Howard C. Taylor, Jr., and Gray H. Twombly. *Am. J. Roentgenol.* 56: 513-522, October 1946.

The authors state that this article is simply a progress report obtained by treating equal and comparable groups of cancer of the cervix by two methods thought at the start to be equally effective.

One group was treated by the "divided dose technic," i.e., twelve treatments of 200 r each to each of six fields, 70 cm target skin distance, 200 kv, 0.5 mm. copper filtration. Along with this, intravaginal x-ray therapy was given three times a week. With the 3- or 4-cm cone, three fields of vaginal irradiation, one directly to the cervix and one to each vaginal vault, were usually possible. Typically, the cervix received four treatments of 500 r each (measured in air) for a total dose of 2,000 r. The parametrial treatments of 750 r each were given through a 3-cm cone pointed into each vault for a total dose of 3,000 r. Two weeks after completion of all roentgen therapy the patient was admitted to the hospital and a radium applicator was inserted into the cervical canal for a dose of 3,000 mc. hours.

The second group received comparable external irradiation—ten treatments of 200 r each to each of six pelvic fields, at 200 or 250 kv. Two weeks after the last treatment the patients were admitted for radium therapy. Four steel sheath needles containing radon gas in gold tubes 2 cm in active length were inserted into the periphery of the cervix, two in front and two in back, the needles of each pair being separated by 1 cm. One centimeter lateral to each of the first needles was placed another 3-cm needle angled out slightly toward the parametria. Finally four needles of 4-cm active length were inserted, two into each side, at a distance from each other and the neighboring 3-cm needles of 1 cm and directed into the parametria at an angle of about 30 degrees. A radon tandem containing an amount of radon approximately equal to that in all the needles combined was then inserted into the cervical canal. The total dose was 6,000 mc. hours approximately 3,000 from the needles and 3,000 from the tandem. In general the needles totaled 100 mc in strength with the tandem amounting to another 100 mc.

Of 113 patients treated with vaginal cones, 54, or 47.8 per cent, were alive and free of cancer when last examined. Of the 94 cases treated with parametrial needles, 26, or 27.7 per cent, were alive and free of cancer. In the first group 39 or 34.5 per cent and in the second group 52 or 53.3 per cent were dead. In the first group 67 were alive, 9 with cancer and 4 possibly with cancer, or 59.3 per cent; in the second group 37 were alive, 7 with cancer and 4 possibly with cancer, 39.4 per cent.

Salutary results were obtained particularly in Hodgkin's disease, lymphosarcoma, and chronic leukemia. Indeed, in the first two disorders dramatic improvement was observed. Some patients fail to benefit from 8-chloroethylamine therapy, and the cause of this failure is not known. Varied responses have been observed in acute and subacute leukemias.

In an impressive proportion of terminal and so-called radiation resistant cases, especially of Hodgkin's disease and lymphosarcoma, the 8-chloroethylamines have produced clinical remissions lasting from weeks to months. There is evidence to suggest that responsive nodes to radiation therapy may occasionally be restored after a course of nitrogen mustard therapy.

The margin of safety in the use of these chemicals is narrow, necessitating the exercise of considerable caution. Great care must be taken in administration to prevent extravasation of the solution or its contact with skin or mucous membranes. The blood picture must be carefully followed at frequent intervals as a guide to subsequent dosage. Immediate local or systemic side effects are relatively inconsequential and can sometimes be avoided or mitigated by careful technique. More serious late toxic effects are concerned with the blood-forming organs and can be largely avoided by adherence to safe dosage schedules.

Although indications and contraindications for the use of the nitrogen mustards remain to be established definitely, it is felt that these agents are deserving of further clinical trial in Hodgkin's disease, lymphosarcoma, and leukemia. Like radiation, they do not cure but offer only symptomatic palliation.

NON-NEOPLASTIC DISEASE

A Comparison of the Effectiveness of Radiation Therapy and Estrogenic Substance in the Management of Hyperthyroidism. Ernest H. Planck. *South M. J.* 39: 794-799, October 1946.

The author reviews briefly the latest theories and schools of thought on the function of the thyroid gland and the development of hyperthyroidism. Methods of treatment of the latter condition and the recent use of estrogenic substance are presented. The basis for the use of massive doses of estrogenic substance is that it produces a depressant effect upon the anterior pituitary body, thereby reducing the production of thyrotropin and thus, indirectly, improving the condition of hyperthyroidism.

A small series of 16 cases, 8 treated by X-ray and 8 by estrogenic substance, is presented with charts showing the average responses in the two groups. X-ray therapy consisted of 1200-1600 r, at 200 kv p, given over two areas of the neck. Estrogenic therapy consisted of 5 mg of diethylstilbestrol given once or twice a week for four weeks, then one dose every two weeks until a total of six months had elapsed. The charts indicate that the estrogenic therapy was more effective. The author also feels that this latter treatment is simpler and less expensive. Two cases are cited in which combined X-ray and estrogenic therapy followed previous thyroidectomies; the estrogenic therapy apparently produced a more decided improvement than the X-ray therapy. Finally, a single case is presented in which estrogenic therapy was used preoperatively with good results.

MORRIS IVER, M.D.

A New Method of Local Treatment of Rheumatoid and Traumatic Affections of the Joints, with Emphasis on a New Approach in the Management of Arthritis and Allied Conditions. Otto C. Kestler. *Geriatrics* 1: 159-163, March-April 1946.

This is a report of 65 patients with arthritis who were treated with radon ointment at the Orthopedic Out-patient Department of the New York Polyclinic Medical School and Hospital. Cases of three types were selected and grouped as follows: (1) the so-called chronic rheumatoid group, including rheumatoid arthritis, peri-arthritis, bursitis, perostitis and epicondylitis, (2) so-called hypertrophic arthritis or osteoarthritis, (3) post-traumatic conditions, including (a) traumatic arthritis, (b) post-traumatic painful atrophies of bones and joints, particularly Sudeck's atrophies or cases similar to Sudeck's atrophies, (c) stiff joints, post-immobilization in plaster of Paris or postoperative cases. Of the 65 patients, 32 were symptom-free after the treatment with radon ointment, 32 were improved, with decrease of pain, 2 noticed no change. No deleterious effects were experienced.

The radon ointment must be sealed onto the area by an airtight bandage. The strength of the ointment used in the cases reported was 200 electrostatic units per cubic centimeter. The quantity depends upon the size of the skin area to be covered, varying from 5 to 30 cc for each treatment. The ointment is squeezed from the tube directly onto the skin and smoothed to a thickness of 1 mm with a wooden spatula. Several layers of gauze cut to a size a little larger than the area of the ointment are then applied, and this is covered with oiled silk or cellophane and sealed with adhesive tape. Applications are made twice a week, and each bandage is kept on for forty-eight hours. The highest number of treatments given to any patient was fourteen. To avoid discouragement, the physician should prepare the patient for possible recurrences or less than complete recovery. Only regular observation and several courses of treatment will give the patient, not a cure, but permanent relief.

Besides producing physiological changes on the irradiated area, the alpha ray therapy results in a hyperemia of therapeutic importance. It manifests itself in an erythema appearing after every application and becoming darker and more pronounced as the use of the radon ointment is continued. The patient should be prepared for this. Sometimes blister formations are observed. In this event, the alpha ray treatments should be interrupted and a reasonable period allowed to elapse before treatment is resumed. These blisters are extremely superficial, similar to those produced by light sunburn, and will disappear with the usual treatment.

Chromoblastomycosis. Report of Two New Cases Observed in the Isthmus of Panama. Carlos Calero. *Arch. Dermat. & Syph.* 54: 265-277, September 1946.

Two new cases of chromoblastomycosis are described by the author, making a total of 154 cases thus far recorded. Both patients were white males. The first showed multiple large crusted verrucae of the foot and leg which had been present for eight years. The second had similar lesions on the hand which had been present for two and one half years. The diagnosis was made by culturing the scabs on Sabouraud's medium and studying the fungi microscopically. The lesions on the

was denied 4 of the 16 patients either because of pulmonary metastases or because they were in such poor condition that they were considered hopeless operative risks. One of these has already been discussed. The other three died within five months from the time they were first seen.

Treatment of Bladder Tumors. Roger W. Barnes, C. LeRoy Turner, and R. Theodore Bergman. *California Med.* 65: 95-97, September 1946.

Properly performed endoscopic electrosection and fulguration is an excellent method of treating bladder tumors, and is preferable to suprapubic removal unless the tumor is more than 5 cm. in diameter or is situated in the ventral portion of the dome of the bladder, in which case the open approach is indicated.

A series of 537 cases of bladder tumors treated during the years 1926 to 1945 is reviewed. Of this number, over a third were discarded because of insufficient data or lack of grading as to malignancy. The remaining cases, 349 in number, were divided into two groups: one treated with electrosection and fulguration, the other receiving, in addition to electrosection, radon implantation. Most of the tumors in the latter group were of grade II malignancy or higher. Radon seeds were usually implanted through the cystoscope four weeks after resection and fulguration of the growth.

On an analysis of those cases which were followed until death it was found that patients with grade II and grade III tumors who were treated with electrosection plus implantation of radon seeds lived longer than those in the group not receiving radiation. The difference is significant for the average length of life from the onset of symptoms to death in the group in which no radon seeds were implanted was approximately two-thirds of that in the irradiated group. This superiority of the combined treatment is borne out by analyses of the group of patients still alive and of the entire series. It has been the authors' experience that the higher the histologic grade of malignancy the poorer the prognosis.

MAURICE D. SACHS, M.D.

Carcinoma of the Penis. Herman Lenowitz and Albert P. Grahm. *J. Urol.* 56: 458-484, October 1946.

One hundred white patients and 39 Negro patients with carcinoma of the penis were studied at Hines Veterans Hospital from 1931 to 1944. The incidence was found to be 5 1/2 times as high in Negro cancer patients as in white, whereas cutaneous carcinoma in general occurs 7 times as frequently in white patients. Of the treated patients (138) 70 are alive and 68 have died. The disquieting finding in this excellent study is the fact that the average time elapsing from the onset of the lesion until admission to the hospital was twenty-one months. Many patients had had ineffectual treatment or the true nature of the lesion had been overlooked.

The study reveals that circumcision, if done early in life, is probably a good prophylactic measure against penile cancers. It was found that the venereal disease rate in these patients was considerably higher than in the general population as shown by U. S. Public Health surveys and control studies on other hospital patients. It was felt that irritation, trauma and chronic inflammation were many times etiologic agents and case reports are included to illustrate this point. Pathologically the lesion is usually a cutaneous cancer and most frequently it is seen in papillary form. In the order of their

frequency of appearance the following sites are listed: (1) frenum and prepuce, (2) glans, and (3) corona. It was deduced that marital status had no effect on the occurrence of cancer of the penis and in no instance did the wife of a patient have carcinoma of the female genital tract.

The usual presenting symptom in these patients is, of course, the presence of a new growth. Other symptoms are pain, a discharge from beneath the prepuce, bleeding, urinary obstruction, increasing phimosis, balanitis, balanoposthitis, urinary fistula and enlargements in the groin. All too frequently the initial lesion is thought to be venereal both by the patient and the physician and is treated as such.

The place of roentgen therapy at Hines Veterans Hospital is an important one. Radium has not proved to be superior in any way and is not ordinarily used. In lesions 2 cm. or less in diameter, not invading Buck's fascia, the treatment is irradiation alone. An adequate dose (about 5,000 r) is delivered in three weeks or less. In larger lesions and in those invading Buck's fascia, surgery is done and preoperative radiation is given to the primary lesion only, in an effort to reduce its size, reduce infection, and to seal off lymphatic channels. 2,000 to 4,000 r are given. No preoperative therapy is given to the inguinal nodes. Postoperative therapy is given to the node-bearing area when block dissection has been done, and it is felt that this therapy is effective in preventing recurrence. Preoperative therapy to lymph nodes is believed to be ineffective in sterilizing the cancer-bearing nodes and to make subsequent surgery more difficult. Lastly roentgen therapy is used palliatively to decrease tumor mass and to control hemorrhage, pain and the foul odor incident to this disease. It was observed that patients gained weight and strength and that many months of comfort could be added to life by such palliative therapy. The authors make no effort to list specific techniques for each set of conditions, but all forms of therapy from 100 kv with 1.0 mm. Al filter at 20 cm. distance to 200 kv with 0.5 mm. Cu filter at 50 cm. distance are used as the condition may require.

Emasculatation is not performed unless the scrotum is directly involved by tumor. Bilateral block dissections of the groin are done when the lesion is large and clinically involved nodes are present on one or both sides.

The authors suggest that improvement in end results might be obtained by reducing the length of the delay period in seeking and obtaining proper treatment for these lesions.

JAMES C. KATTERJOHN, M.D.

Nitrogen Mustard Therapy. Use of Methyl-Bis (Beta-Chloroethyl)amine Hydrochloride and Tris (Beta-Chloroethyl)amine Hydrochloride for Hodgkin's Disease, Lymphosarcoma, Leukemia, and Certain Allied and Miscellaneous Disorders. Louis S. Goodman, Maxwell M. Wintrobe, William Dameshek, Morton J. Goodman, Alfred Gilman and Margaret T. McLennan. *J. A. M. A.* 132: 126-132, Sept. 21, 1946.

In this preliminary communication the authors present the clinical results obtained for 67 patients treated intravenously with the nitrogen mustards (halogenated alkyl amine hydrochlorides) for Hodgkin's disease, lymphosarcoma, leukemia and certain related and miscellaneous diseases. Complete reports including pathologic observations and detailed hematologic data will be published later.

7 000 r at the surface The dose at 0.25 cm was approximately 2,000 r, and at 0.5 cm 600 r, under these conditions In order to assess this dosage, minimal erythemas on 1 sq cm of skin were compared with that produced by x rays at 180 kv p F S D 40 cm h v l 0.9 mm Cu It was found that 750 r of beta rays produced erythemas equivalent to those produced by 700 r, of x-rays

The authors conclude that radiations from beta ray plaques can be satisfactorily measured by ionization methods Such plaques give a stable output over a period of years and may be used successfully for superficial lesions where no more than 30 per cent depth dose is needed at 0.25 cm Such lesions are shallow rodent ulcers, port wine marks, and hyperkeratoses In terms of depth dose beta radiation corresponds to "grenz" rays generated at 25 kv, but its energies and ranges are equivalent to those of secondary electrons released by homogeneous x rays of some 1.6 mv energy

SIDNEY J HAWLEY, M D

New Units for the Measurement of Radioactivity
E U Condon and L F Curtiss Brit J Radiol 19 368, September 1946

As the curie is defined as that amount of radon in equilibrium with one gram of radium, it should be used only to represent the disintegration in the radium family A new and more suitable unit is proposed the "rutherford," abbreviated "rd," which may be used for any radioactive disintegration The rutherford is 10^6 disintegrations per second A micro-rutherford thus would be one disintegration per second This is readily remembered, easily measured, and is of sufficient difference in size from the curie so that no confusion would result

For the measurement of gamma-ray sources the roentgen-per-hour at one meter is suggested This would be abbreviated rhm and pronounced 'rum' The gamma ray strength of any source of 1 rhm is 1.18 times that of 1 curie

SIDNEY J HAWLEY, M D

EFFECTS OF RADIATION

Pathologic Effects of an Instantaneous Dose of Radiation Shields Warren Cancer Research 6 449-453, September 1946

The distinctive feature of the atomic bomb is the large amount of radiant energy that it produces While this energy covers a wide range of the electromagnetic spectrum, its chief physiologic and pathologic results may be divided into two groups first the effects of heat (primary thermal injury of the flash burn type and secondary thermal injuries due to induced fires), second the effects of short wave radiation and neutrons paralleling closely the effects made familiar by experimental studies of the biologic effects of x rays Combined with and modifying and obscuring these injuries are the more usual effects of the conventional type of bomb chief among which are injuries due to flying debris or impact against fixed structures

In the studies of the atomic bomb effects at Nagasaki and Hiroshima carried out under the direction of the Naval Medical Research Institute particular attention was given to the injuries due to radiation The immediate effects were manifested as weakness malaise fever and often death, and appeared usually within forty-eight hours, while the delayed effects manifested themselves in a variety of ways

Unfortunately the disorganization of the Japanese was so great that no adequate material exists to determine the exact nature of immediate effects The present study dealing with the later effects is based on a cursory survey of 13 000 survivors

There were three chief somewhat overlapping symptom complexes due to damage to the hematopoietic tissue The first was the leukopenic group in which infection particularly Ludwig's angina was the outstanding manifestation The great bulk of leukopenic deaths occurred during the first three weeks following the bombing According to the studies of the Japanese investigators the leukocytes in the circulating blood were destroyed at the same time the hematopoietic system was damaged so that white blood cell counts as low as 200 per cu mm were found in the first few days

From three to five weeks after the bombing a considerable number of hemorrhagic deaths occurred associated with thrombocytopenia induced by radiation

damage to the megakaryocytes of the bone marrow It is suggested that the blood platelets in the circulation were not destroyed by the radiation and that only a low point was reached as a result of deficiency in blood did hemorrhagic manifestation occur

Those with serious bone marrow damage who weathered the first few weeks showed later anemic manifestations with red blood cell counts in some instances dropping to one million or below

As would be expected, the gonadal effect was much more prominent in case of the testis than of the ovary Ova were present in the ovaries in many cases only occasionally in women of the child bearing age did atrophy occur However, it was relatively unusual to find a recent corpus hemorrhagicum or corpus luteum In the testis, on the other hand in men who had been exposed to appreciable amounts of radiation atrophy of the germinal epithelium was striking

No deleterious effects from residual radioactivity could be found in persons who had entered the bombed areas soon after the explosion and remained there

Radiation Effects of the Atomic Bomb Among the Natives of Nagasaki, Kyushu. James S P Beck and William A Meissner Am J Clin Path 16 583-592 September 1946

Some of the radiation effects of atomic bombing among the natives of Nagasaki are reported Among 20 patients whose blood or bone marrow was studied there were anemia neutropenia, and thrombocytopenia or depression of the marrow In 7 postmortem examinations there was confirmatory evidence of damage to the bone marrow Evidence of recovery of bone marrow was observed both clinically and at necropsy Histologic evidence of lipid depletion of cells of the adrenal cortex was found Aspermatogenesis was noted in some instances The mortality rate could have been lowered by adequate medical care

Radium Dial Painting—Medical Status of Workers Irving R Tabershaw J Indust Hyg & Toxicol 28 212-216 September 1946

A survey was made of 52 radium dial painters employed a minimum of eighteen months A history

leg were treated solely by roentgen rays. From Dec 22 1944, to April 4, 1945, a total of 11,700 r was given to the areas. A filter of 2 mm of copper and 1 mm of aluminum was used, but the voltage and distance factors are not given.

The lesions on the hand were treated by electrocautery and ten irradiations totaling 1 000 r were given to the area. The author is not sure that a full cure was obtained in the case receiving x-ray therapy (the patient was not seen following discharge from the hospital), but he believes that the case treated surgically was completely cured.

JOSEPH T RANZER M D

DOSAGE

Dose Measurements with Radium Beta-Ray Applicators G J Neary Brit J Radiol 19 357-367, September 1946

With the development of the betatron it seems likely that therapy with fast electrons will become available, so that the study of beta ray applicators is in order. This type of applicator, designed for the therapeutic utilization of the primary beta radiation of radium, has not been much used in recent years and consequently has received little physical study. The old belief that beta rays were caustic arose because unscreened plaques were used for their gamma ray effect, with the result that large beta ray doses were delivered superficially. The caustic effect actually is due to this excessive dosage rather than to any qualitative effect of the rays.

The maximum effective range of beta radiation is about 1.5 cm in material of unit density. New plaques reach equilibrium in about five weeks, but the output may rise slowly for years.

Since gamma radiation produces ionization by the intermediate agency of beta particles, it seems reasonable to measure primary beta radiation like gamma radiation by air ionization corrected to standard conditions of temperature and pressure. The quantity thus determined expressed in esu per cc is termed the dose of beta radiation in roentgens. Because the dose rates of the applicators are high and the decrease with distance is great, very shallow chambers are necessary for measurement. As beta rays ionize air directly there is no question of wall effect. It is only necessary that the walls should not absorb an appreciable amount of the radiation.

Under the conditions of measurement the gamma ray component is measured also. However the gamma ray effect near the surface is only a small fraction of the beta ray component. At greater depths where the relative importance of gamma rays enters into consideration due to the absorption of beta rays by the additional material around the chamber the gamma-ray component more nearly governs the dose rate.

The thickness of the ionization chamber affects measurements at the upper surface of the phantom. For distances closer than 0.75 mm the dose is obtained by extrapolation.

Applicators having 5 mg of radium element per sq cm usually show a surface dose rate of the order of 5 000 r/hr. There is little effect of size, for the oblique filtration is so marked that it cuts out practically all the radiation except that coming from a small area near the point being measured. A concomitant effect is that the dose rate is practically uniform over most of the area of the applicator provided the radium loading

is uniform. For the same reason, depth doses do not vary as much as would be expected with the size of the applicator. For example a comparison at the depth of 1 mm shows only 15 per cent greater depth dose from an applicator with a diameter of 2 cm than from one of 1 cm diameter.

Surface dose rates varied irregularly with similar applicators. This variation parallels the beta gamma ray ratio which was found to be about 2 to 1 for high output applicators. High-output applicators were found to have low inherent filtration. Relatively more "soft" radiation was found from the high-output applicators and there was progressive hardening as the inherent filtration was increased. These differences were found to be due chiefly to differences in the composition of the radium salt mixture. The type of backing and the degree of equilibrium reached by radium E will also affect the strength. Thus for various reasons it is not sufficient with beta ray applicators to rely on the radium content and distribution, but each applicator must be measured.

The most striking observation in depth-dose measurement is the rapid fall with increasing depth, namely to about 50 per cent at 1 mm. There is little difference in depth percentages with different filters except that 0.1 mm of lead approximately doubles the depth dose at 4 mm, but at the expense of a fourfold reduction in the surface dose. Absorption was shown to have much more effect on the fall in depth dose than distance. Back-scatter appears to have only a small influence, probably less than 10 per cent.

Studies were made on absorption and reflection effects of beta radiation by measurements with radium (B plus C) and radium E sources. The specific beta ray dose rate at zero filtration is 1,180 r/mc.hr for radium (B plus C) and 525 r/mc.hr for radium E and 1 710 r/mc.hr for radium in final equilibrium excluding the soft radiation from radium D.

SYDNEY J HAWLEY M D

Dose Measurement in Beta-Ray Therapy G W Bloomfield and F W Spiers Brit J Radiol 19 349-356 September 1946

Studies were made of the dose from beta ray plaques by means of a small condenser ionization chamber and wax and water phantoms. The unit of dosage used was esu/cc, called for the authors' purposes a 'roentgen'. Two plaques of somewhat different construction were investigated. A comparison of the measurements obtained with measurements made by Neary with a different type of apparatus shows good agreement at distances of 1 mm or more from the plaque. Nearer the plaque surface the design of the ionization chamber and the position of the plaque affect slightly the accuracy of the measurements.

A study was also made of the dose delivered when a reflector was used to cover a greater area after the manner of a beta ray 'bomb'. Observations with plane and elliptical reflectors showed that the increase in dose was less than had previously been reported. The use of reflectors therefore seems to be more of a convenience than an economy. Depth dose measurements in water phantoms also failed to show any significant difference between contact positions and with reflectors. The depth dose was found to drop to 50 per cent at 1.5 mm and to 20 per cent at 3.3 mm.

In practice it was found that superficial rodent ulcers were cured by a beta ray plaque with doses of 6 000 to

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The Plutonium Project

Introduction to a Symposium Presented at the Thirty-Second Annual Meeting of
the Radiological Society of North America, Chicago, Ill, Dec 1-6, 1946

RAYMOND E ZIRKLE, Ph D

University of Chicago

THE Plutonium Project was assigned the task of making and purifying the artificial element plutonium for use in atomic bombs. The method of making plutonium utilized the nuclear reaction between neutrons and uranium²³⁸, the neutrons being excess from a so-called nuclear chain reaction maintained by other neutrons and uranium²³⁵. The uranium²³⁸ and uranium²³⁵ were not separated. They were in their natural mixed condition.

The fact that the chain reaction was used meant that according to pre-war standards fantastic amounts of gamma rays and fast and slow neutrons would be emitted in a chain reactor of any considerable magnitude. We were familiar, to a certain extent, with these radiations before the war, but we had had no experience whatever with the large amounts anticipated in a chain reactor.

In addition to the tremendous potential hazards due to the radiations emitted in the chain reaction, there were also enormous hazards to be anticipated in the purification of the plutonium, since plutonium was formed in masses of uranium and had to be separated from that element. Moreover, included in this mixture was a large variety of so-called fission products formed in the fission of uranium²³⁵ after its absorption of a neutron. These fission products are highly diverse in

their chemical natures and in the types and energies of the radiations which they emit. They are all radioactive. Consequently, it was rightly anticipated that, unless stringent control measures were set up, it would be very easy for personnel to take into the body, by ingestion, inhalation, or through wounds, certain of these fission products, to say nothing of plutonium itself, which is also radioactive.

It was early recognized in the Project not only that control measures must be set up but that it might be an excellent idea to carry out extensive and, so far as possible, intensive radiobiological research with a view to learning how hazardous the various radiations are, to what degree the dangerous radioactive substances may be taken into the body by various routes, how long they stay in the body, where they stay while there, and how dangerous any definite amount thus retained may be.

The radiobiological work of the Plutonium Project was carried out at various sites. During the war all of these sites were under the direction of one of your colleagues whom you know well—Dr Robert S Stone. The sites where most of the research was carried out were the University of California, the Metallurgical Laboratory of the University of Chicago, which is now the Argonne National Laboratory, Clinton Laboratories near Oak

was taken of each individual, the physical and dental condition, blood counts and nutritional status were determined, and these findings were correlated with breath radon analyses. Results of this survey again emphasize that careful attention to the hazards of radium in dial painting is necessary and that an educational campaign regarding working habits, personal

hygiene and attention to the teeth and blood must be stressed. No deleterious effects may be expected within a year and a half to four years of employment when the radium content of the body is kept below 0.1 microgram. Reliance on medical examination is not an adequate safeguard, analysis of breath radon is practical and reliable.

EXPERIMENTAL STUDIES

Experimental Radiotherapeutics Joseph S. Mitchell. *Schweiz. med. Wchnschr.* 76: 883-889, Sept. 16, 1946.

This article is an abstract of the recent advances in research on the mechanisms of radiotherapeutic effects presented at the British-Swiss Medical Conference at Basle. These advances are ascribed to improved methods of employing radioactive tracers and to advances in cytology, cytochemistry, genetics, and nuclear physics. The author considers the following of special interest: the inhibition of thymonucleic acid synthesis by raditions, the significance of chromosome breakage, the dependence of biologic efficiency on specific ionization, the production of artificial gamma ray sources for therapy, and the possible applications of radioactive isotopes, high-energy gamma radiations, and fast neutrons. The article is so condensed as to be intelligible only with difficulty, but has a bibliography to which liberal reference is made for those who wish fuller discussion. LEWIS G. JACOBS, M.D.

Influence of Wave-Lengths on Certain Lesions Produced by the Irradiation of Mice A. Lacassagne. *Proc. Roy. Soc. Med.* 39: 605-612, August 1946.

This author describes the results of treatment of mice with K radiation of molybdenum, ultraviolet rays, and L radiation of silver. The objective in using the K radiation of molybdenum was the production of complete sterilization of female mice two months old. These mice were treated with unfiltered rays with an effective wave length of 0.95 Å at 35 kv p, 15 ma. and focal skin distance of 12 cm. The dosage rate was 3,000 r per minute. Two areas 1 cm square on the dorsal surface of each mouse, centered as close as possible over the ovaries, were treated. Four groups of mice were used receiving 3,000, 4,500, 6,000, and 9,000 r respectively. Two mice of the 6,000 r group and all of the 9,000 r group died less than nine weeks later.

The only cutaneous reaction which followed these dosages was the loss of hair over the exposed areas occurring about the twentieth day regardless of the dose. In no case was there any sign of ulceration. A sparse regrowth of hair occurred in the animals receiving the smaller doses. In a few there was slight sclerosis of the fatty tissue and some atrophy of the cutaneous muscle. In only a small proportion was complete sterilization accomplished. In only 3 of 11 mice that survived was there total atrophy of both ovaries. All of these had received 4,500 r or more. In most cases it was impossible because of the smallness of the test object to exactly center both ovaries and unilateral ovarian atrophy resulted. Histologic studies showed almost complete destruction of the follicles and the parenchyma was riddled with cavities cystic in nature.

In addition to the changes in the ovaries, some of

these mice showed extreme atrophy of the lower pole of the kidney, undoubtedly due to the radiation. Histologic study of these affected kidneys showed most of the destructive effect to be in convoluted tubules. The glomeruli as a rule appeared intact and seemed to be capable of functioning, but since the tubules were destroyed and there was no place for the infiltrating liquid to escape, it distended the capsules. The irradiated area therefore assumed somewhat the appearance of a polycystic kidney. There was thus demonstrated a definite difference between the extreme sensitivity of the epithelial cells and the apparent integrity of the vascular formations.

Ultraviolet rays in large dosage (1,500 mms) produced a necrotic dermatitis with edema beyond the irradiation area within a few hours. Following this was an intense erythema lasting five to six days. Histologic examination of the skin showed rapid local necrosis involving every variety of cell. The destruction is not deep seated, however, and the repair process is rapid and early.

The L radiation of silver was generated by a tube operated at 45 kv p and 15 ma, with a thin window of aluminum. A dose of 500 ergs per square millimeter produced a lesion macroscopically comparable to that obtained with 1,500 f of ultraviolet rays. This was given to 11 young mice. Reactions were less rapid and severe than those produced by ultraviolet rays. There was a pronounced erythema on the third day followed by pigmentation. On the eighth day there was severe desquamation followed by superficial ulceration and a scab on about the twelfth day. This separated on the sixteenth day, exposing a red, smooth and hairless epidermis. Regrowth of hair began on the thirtieth day.

Histologic study showed cellular changes which started very early but affected only certain elements sensitive to radiation. This selective action was confined to the invaginations of the epidermis which were to constitute the hair follicles. Many of these showed signs of advanced degeneration, whereas the epidermis showed no more than a simple cellular swelling and the dermis no reaction. Cornification of the whole epidermis and degeneration of the follicular buds was advanced on the fifth day. On the ninth day the degeneration of the whole epidermis was complete. By the eleventh day a smooth thin epidermis had formed under the skin. This selective action of the rays on the cells of the germinative process agrees with previous accounts of epidermitis due to irradiation but differs markedly from the diffuse necrosis produced by ultraviolet rays.

In conclusion, this author has shown that there is a distinct difference in the cutaneous response to radiations of radically different wave lengths when a comparable quantity of each of the radiations is used.

BERNARD S. KALAYJIAN, M.D.

Components of the Acute Lethal Action of Slow Neutrons¹

RAYMOND E. ZIRKLE, Ph.D

University of Chicago

EARLY IN the history of the Plutonium Project, months before the first chain reacting pile was built, it was realized that both fast and slow neutrons would leak from any operating pile of finite dimensions and thus constitute radiation hazards

Fast neutrons, of course, were not a new radiobiological agent in 1942, reports of their various biological effects had been accumulating since 1935

With slow neutrons, however, there had been no radiobiological experience, because the earlier sources of neutrons, such as cyclotrons, had not been suitable for such investigations. Certain it was that slow neutrons would have radiobiological action, because it was known that slow neutrons were captured by and would react with the nuclei of many of the kinds of atoms found in tissues, each of these nuclear reactions was known to produce ionizing particles by some means, direct or indirect, and in many cases a significant fraction of the ionizing energy of these particles was certain to be absorbed in the nearby tissues

For each of these nuclear reactions, data were available concerning the probability that the reaction would occur, and if it did, how much radiation energy would be released and what types of ionizing particles would be produced

Also, from the extensive literature of general radiobiology then in existence, there was a fair knowledge of the relative effectiveness of the various kinds of ionizing particles in producing injury. Accordingly, it was possible to calculate the effectiveness of a given number of slow neutrons absorbed by the body, if one were satisfied with two implicit assump-

tions first, that we were aware of all of the nuclear reactions of slow neutrons with the various atomic species in the body, second, that the effectiveness of the various types of ionizing particles was not affected by some unknown physical mechanism or by the peculiarities of their places of production and absorption

In view of these two uncertainties, it was considered desirable to compare the calculations of effectiveness against direct measurement. The principle of such a comparison is very simple first, expose samples of some certain biological object to graded doses of slow neutrons and thus determine the number of slow neutrons which must be captured in order to produce a given amount of biological effect, second, compare the number so determined with the number predicted by calculation to be necessary to produce the same amount of biological effect

The experiments were carried out at Clinton Laboratories, Oak Ridge, Tennessee, in 1944, with the collaboration of Dr J R Raper and the assistance of Mr E F Riley and Mr G E Stapleton. The biological effect studied was acute lethal action on mice

The shield of the Clinton pile was constructed with two tunnels so located that animals could be placed on a special carriage and pushed inside the shield to a position where they were exposed to the neutrons leaking from the pile proper. Mice were exposed in groups of twenty-four in a special bismuth container mounted on a tunnel carriage. The bismuth was so arranged as to shield the entire group of mice from gamma rays emitted from the materials of the carriage

¹ This paper is a brief version of a longer report to appear in the Plutonium Project Record of the Manhattan Project Technical Series. The work was done at Clinton Laboratories, near Oak Ridge, Tennessee, under Contract W-7405-eng-39 of the Manhattan District. Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946

Ridge, Tennessee, and the National Cancer Institute

I might also point out that the Plutonium Project was only one part of the gigantic Manhattan District and that other radiobiological work was carried on in the District aside from that in the

Plutonium Project, the most active sites being at the University of Rochester and at Columbia University

The papers in the present Symposium represent a small portion of the total radiobiological results obtained at the various sites of the Plutonium Project

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Introducción al Certamen sobre el Plutonio

El Proyecto del Plutonio representa la parte del gigantesco "Distrito de Manhattan," dedicada a la producción y purificación del elemento artificial plutonio para empleo en las bombas atómicas. En relación con el proyecto se inició un plan

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activity to the total 50 per cent survival dose was equivalent to only 10/9 or about 1 n-unit

5 *Other mechanisms* leading to production of ionization tracks in the mice were also known, but these could be shown to be quite small in comparison to the four just described

The various contributions to the total 50 per cent survival dose may now be added up in terms of the biological effectiveness of the n-unit of fast neutrons (1) the fast neutron contamination of the slow neutrons, 45 n, (2) capture gamma rays, 9 n, (3) the reaction $N^{14}(n,p)C^{14}$, 54 to 68 n, radioactivity, 1 n. The total lies between 109 and 123 n

This result is to be compared with the 50 per cent survival dose of fast neutrons alone. This dose, in earlier experiments with the same strain of mice, had been found to be 91 n. However, the earlier experiments had been carried out with a dose rate about ten times higher than that used in the slow neutron experiments. Under very similar conditions involving the same strain of mice and two dose rates of gamma rays, Henshaw and co-workers (see page 349) found the higher

dose rate was 1.37 times as lethal as the lower. The LD50 of 91 n is accordingly to be multiplied by 1.37, thus giving 124 n as the fast neutron dose to be compared with the combined dose which has been calculated above to be biologically equivalent to between 109 and 123 n

The agreement of the two values might tempt one to a conclusion that the lethal action of the slow neutrons has been completely accounted for in terms of the physical events known to take place. However, the measurements involved in these experiments must be regarded as preliminary, a much better job can be done with improved technic now known to be feasible. The possible inaccuracy is great enough that, so far as we know, some unknown mechanism might contribute to the total lethal action to perhaps the same extent as the capture gamma rays. However, the results would seem to exclude the possibility and the fear of there being some unknown mechanism which creates a hazard far greater than that due to the known mechanisms

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University of Chicago
Chicago 37, Ill

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Componentes de la Acción Letal Aguda de los Neutrones Lentos

Varios grupos de ratones fueron expuestos a dosis graduadas de neutrones lentos. Trazando en una gráfica, frente a la dosis, el número de animales que sobrevivían por tres semanas, se obtuvo una curva que revelaba la dosis de sobrevivencia de 50 por ciento. En las condiciones del experimento, la dosis de neutrones lentos se asociaba con ciertas dosis *parciales* calculables debidas a elementos yonizantes de distintos orígenes, y en particular neutrones veloces, rayos gamma procedentes de reacciones de captura, protones y núcleos de carbono producidos por la transmutación de nitrógeno corporal y radioactividad evocada por la captura de

neutrones por ciertos elementos del cuerpo. La suma de esos varios aportes a la dosis de sobrevivencia, expresada en términos de la efectividad biológica de la unidad-*n* de neutrones veloces, se aproximó muy de cerca a la dosis de sobrevivencia de 50 por ciento de neutrones veloces, obtenida en los experimentos anteriores en ratones de la misma raza. Por consiguiente, aunque las mediciones realizadas entrañan algunas inexactitudes, el resultado parece excluir la posibilidad de que algún mecanismo desconocido intervenga en la acción de los neutrones lentos y cree un peligro muy superior al debido a los mecanismos conocidos

when they captured neutrons and also to shield each animal from gamma rays emitted by its neighbors. Bismuth itself emits relatively very few gamma rays under these conditions.

The various groups of mice were exposed to graded doses of slow neutrons as determined by measuring the radioactivity induced in suitable metal foils. The number of mice surviving for three weeks was plotted against dose, and the resulting curve showed that the 50 per cent survival dose was 4.2×10^{12} slow neutrons per square centimeter of mouse.

This dose of slow neutrons, under the conditions of the experiment, was associated with the following measurable and calculable *partial* doses due to ionizing agents of various origin:

1 *Fast neutrons* Under the conditions of the experiment, the slow neutrons were badly contaminated with fast neutrons. These were measured directly in n-units in the usual way. (The n is the amount of fast neutron radiation which produces one scale reading of a Victoreen r-meter equipped with a standard 100 r chamber.) The dose of fast neutrons which accompanied 4.2×10^{12} slow neutrons per square centimeter was 45 n.

2 *Gamma rays*, almost entirely originating in capture reactions. The chief of these reactions was capture of neutrons by hydrogen nuclei to form deuterium nuclei plus gamma rays. The dose of gamma rays associated with 4.2×10^{12} neutrons per square centimeter was calculated to be 84 r.

In an earlier experiment it had been found that gamma rays and fast neutrons are additive in producing acute lethal action on mice, but that 1 n of fast neutrons was lethally equivalent to 9.2 r of gamma rays. Accordingly, the 84 r of gamma rays due to capture reactions could be considered equivalent to $84/9.2$ or 9 n of fast neutrons.

3 *Protons and carbon nuclei* produced by the transmutation of body nitrogen. Nitrogen¹⁴ plus a neutron yields a fast proton and a fast nucleus of carbon¹⁴.

These two ionizing particles fly apart from the point at which the nitrogen nucleus captures the neutron, they produce ionization tracks very similar to those produced by the atomic nuclei ejected from body atoms by fast neutrons and therefore can be considered to have the same biological effectiveness per unit of energy absorbed.

Since the kinetic energies of the proton and carbon nucleus are known and the probability of their production by neutron capture is also known, it is possible to calculate the total energy absorbed by the tissues from these ionizing particles and hence to calculate in roentgen equivalents the dose of them received by a mouse during an exposure which results in 50 per cent survival. This dose turned out to be 136 roentgen equivalents. For comparison with the fast neutron and gamma ray contributions described above, it is desirable to express these 136 roentgen equivalents in n-units. The number of roentgen equivalents in one n has never been accurately determined, it is currently considered to have a value between 2 and 2.5. Dividing 136 by these two limiting numbers, we find that the biological effectiveness of the protons and carbon nuclei from the nitrogen transmutation is equivalent to between 54 and 68 n of fast neutrons.

4 *Radioactivity* is induced through neutron capture by certain body elements, and a fair fraction of the radioactive substances so formed stay in the body long enough to irradiate it. The radioactivity produced in the mammalian body by a known amount of slow neutron bombardment has been determined by Dr. Howard Curtis and Dr. Joseph Teresi, this makes it possible to calculate the dose of beta and gamma radiation resulting from the radioactivity produced by an exposure resulting in 50 per cent survival. This dose turned out to be somewhat less than 10 roentgen equivalents. Since a roentgen of beta and gamma rays, as already mentioned above, was known to be only about one-ninth as effective as an n-unit of fast neutrons, then the contribution of radio-

activity to the total 50 per cent survival dose was equivalent to only 10/9 or about 1 n-unit

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Biological Studies in the Tolerance Range¹

EGON LORENZ, Ph D, W E. HESTON, Ph D, ALLEN B ESCHENBRENNER, M D

and

MARGARET K DERINGER, Ph.D,

National Cancer Institute, Bethesda, Md.

THE experiments to be discussed here were started early in 1941 and were greatly expanded during the war. Although they are not yet completed, it is not expected that the results will be altered significantly by future findings.

Gamma rays were used throughout the experiments. The daily doses were 88 r, 44 r, 22 r, 11 r, and 0.11 r, given either in eight hours or twenty-four hours per day. Three radiation sources were used: 1 gm, 250 mg, and 100 mg of Ra element filtered with 0.5 mm of platinum. The shelves carrying the cages of the experimental animals were arranged so that each cage in a given set was approximately at an equal distance from the source for each exposure level. Figure 1 shows the experimental set-up used with the 1 gm source. After the daily eight-hour exposure, the source was lowered underground into a shaft to a depth of 21 feet. In the two other experimental set-ups the shelves for animal cages were arranged similarly. The gamma ray sources were kept in lead boxes provided with hinged lids. Doses were measured at several places within each cage with calibrated 0.25 r and 25 r Victoreen ionization chambers. The error of the dose varied with the size of the cages. It was estimated to be ± 10 per cent in the mouse and guinea-pig cages, the average total dose for each animal can be expressed by the dose measured in air. The average total dose received by the rabbits was probably smaller by 25 per cent than the dose as measured in air in the middle of the rabbit cages.

Three inbred strains of mice were used

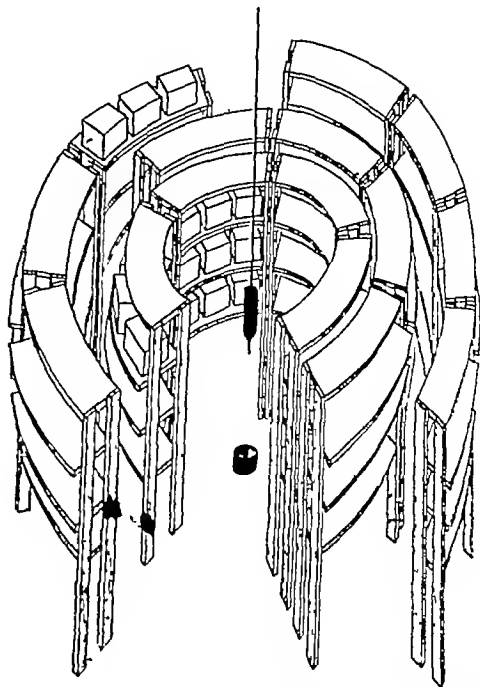
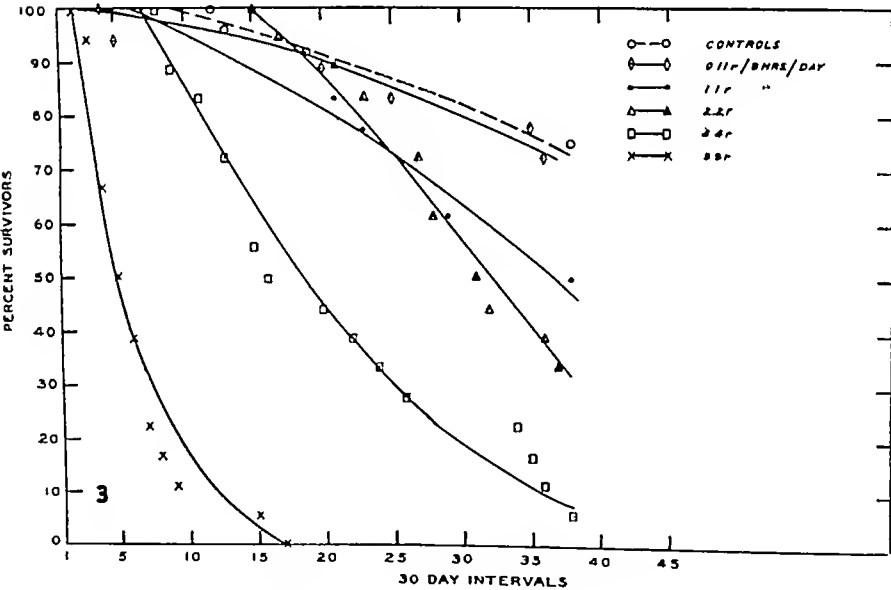
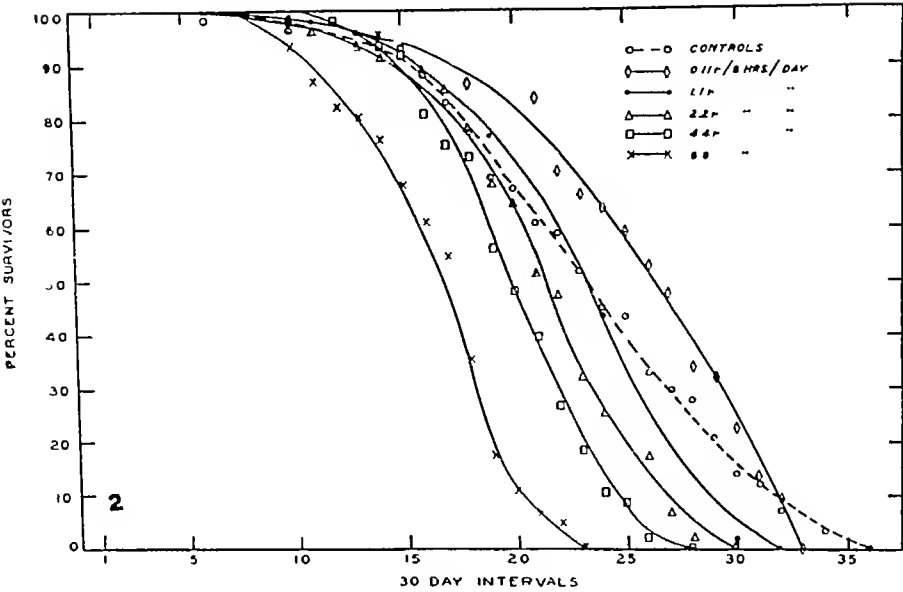


Fig 1 Arrangement for irradiation of experimental animals eight hours daily

in the experiments, strain A, C3H, dba and LAF₁ hybrids, these latter animals also being genetically homogeneous. The guinea-pigs used were genetically heterogeneous hybrids and two inbred strains. The rabbits were crosses of Dutch and American Blues.

The exposures were started at the age of two to three months for the mice, three to six months for the guinea-pigs, and five months for the rabbits, the animals were exposed daily until *in extremis* or dead, with the exception of those used in term exposures. Blood counts were taken every four weeks at the beginning and

¹ The work reported herein was done at the National Cancer Institute as part of the program of the Metallurgical Laboratory, University of Chicago, under the Manhattan Project. This paper is a brief version of material to be published in the Plutonium Project Record of the Manhattan Project Technical Series. Presented at the Thirty second Annual Meeting of the Radiological Society of North America Chicago Ill Dec. 1-6 1946



Figs 2 and 3 Percentage of survivors vs time for mice (Fig 2) and guinea-pigs (Fig 3)

more frequently in the later stages of the experiments. The highest accumulated doses were 5,900 r for mice, and are at present 6,000 r for guinea-pigs and 12,000 r (air) for rabbits.

Figure 2 shows the percentage survival of LAF₁ mice per thirty-day intervals. The animals of the 8.8 r group from the beginning show an increased mortality rate in comparison with untreated controls. In the lower exposure groups, the increase

in mortality rate begins later, the smaller the daily dose. The decreased initial slope of the curve for the animals of the 0.11 r group may be attributable to biological variations or may indicate a general stimulating effect of an obscure mechanism of the radiation. However, the death rate increases later and the slope of this curve increases over that of the control curve, indicating that the destructive action of the radiation is cumulative, even

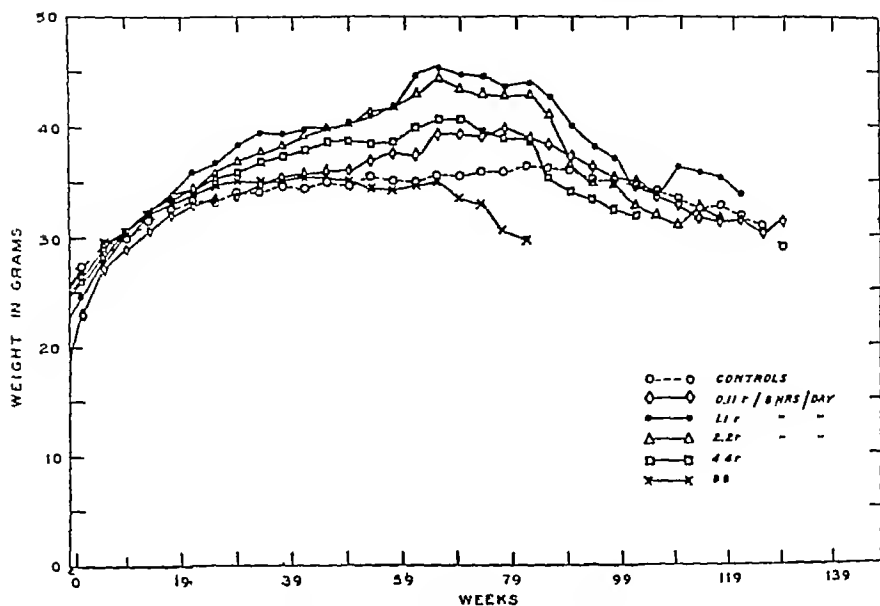


Fig 4. Weight curves for male mice.

for such small doses as 0.11 r given in eight hours per day

There is no predominant syndrome of radiation death for mice at any of the dose levels used. In guinea-pigs, on the other hand, radiation death is uniformly caused by anemia and thrombocytopenia. This has occurred so far only in the animals given 8.8 r, 4.4 r, and 2.2 r in eight hours per day.

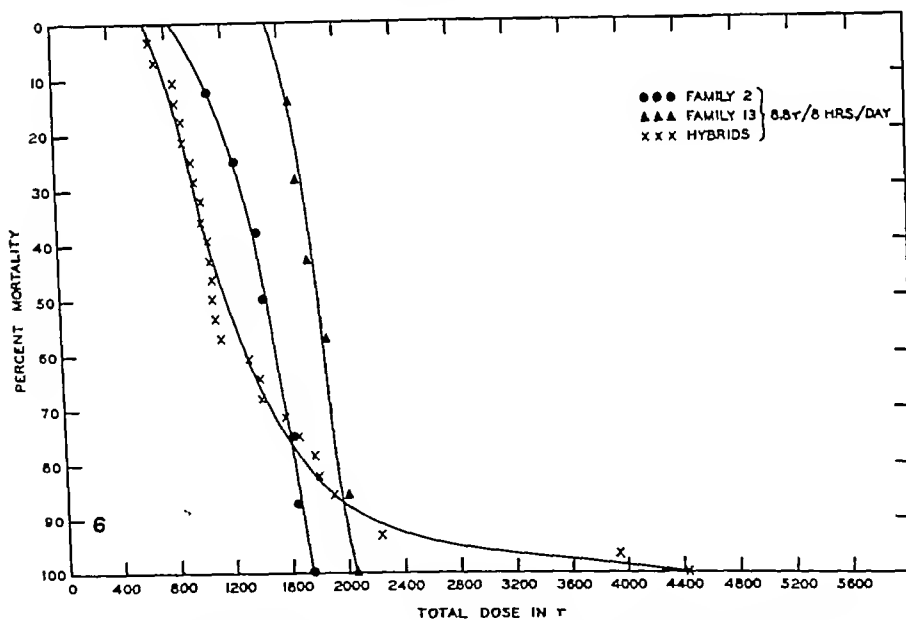
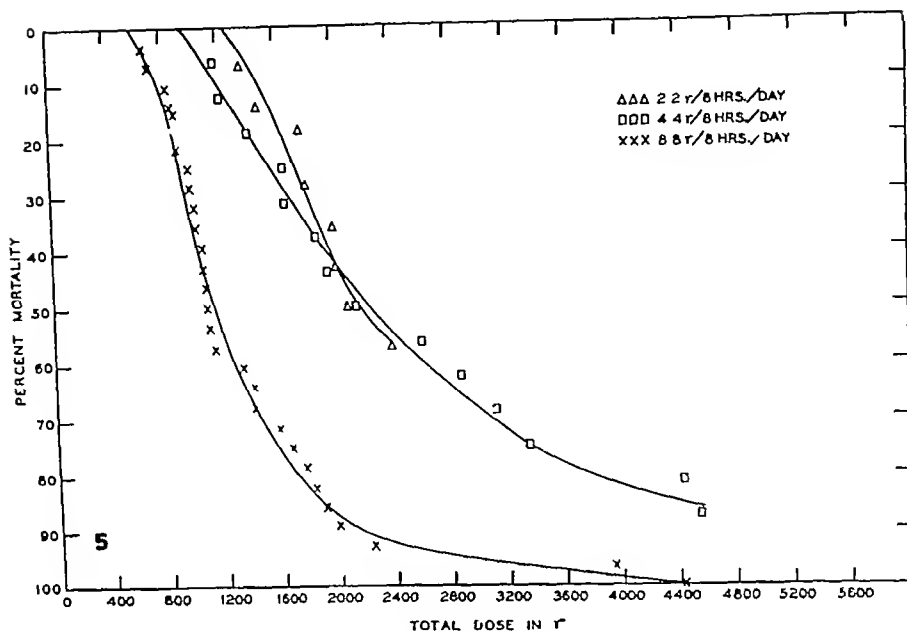
Figure 3 shows the mortality curves for the hybrid guinea-pigs. The lethal dose for the guinea-pigs of the 8.8 r exposure level ranges from 600 to 4,400 r. At all levels, with the exception of 0.11 r, there is a considerable decrease in life span. As a number of animals are still alive at the lower levels, conclusions are restricted to those which have died. No conclusions can be drawn as to the life span of the rabbits, as only 3 animals were used on each level and too few have died.

In discussing the mortality curve it was pointed out that the data may indicate an initial stimulating effect of chronic irradiation for the animals exposed to 0.11 r. A stimulating effect is also indicated by changes in the weight of the animals. Figure 4 gives the weight curves of the irradiated LAF₁ mice. A weight increase

over that of non-irradiated controls was observed in all irradiated groups with the exception of that exposed to 8.8 r. It is most striking in the animals exposed to 1.1 r, in which the average weight increased by about 50 per cent over that of the controls after approximately sixty-nine weeks of exposure. This weight increase is mainly due to an accumulation of abdominal fat. It is present in both males and females and also in the guinea-pigs, and probably in the rabbits, although the limited number of animals makes this last conclusion questionable. The increase in weight of the males at the 1.1 r level cannot be likened to a castration effect, since the testes of the animals show but little damage, while the females at this level, which are sterile after sixty-nine weeks of exposure, show a less pronounced weight increase. No explanation can be offered for this phenomenon.

Radiation damage to the hematopoietic system will be discussed by Dr. Jacobson in another paper.² It suffices to say here that the blood-forming organs of rabbits and mice are extremely resistant to the effects of chronic irradiation and the peripheral blood picture shows little change

² See page 286



Figs 5 and 6 Mortality from anemia and thrombocytopenia for hybrid guinea-pigs (Fig 5) and for hybrid and two inbred strains of guinea pigs (Fig 6)

except in those animals in which leukemia develops. This is corroborated by the pathological data on the blood-forming organs, which show little radiation injury. Even for the highest accumulated doses, over 5,000 r, the bone marrow of mice (with the exception of those which showed leukemic infiltration) was normal. In contrast to mice and rabbits, the effect

of radiation upon the hematopoietic system of the guinea-pig is pronounced, resulting in death from anemia and thrombocytopenia. This was manifested by patchy ecchymoses, especially of the proximal part of the small intestine. Figure 5 shows the mortality curves resulting from anemia and thrombocytopenia in animals exposed to 8.8 r, 4.4 r, and 2.2 r. No

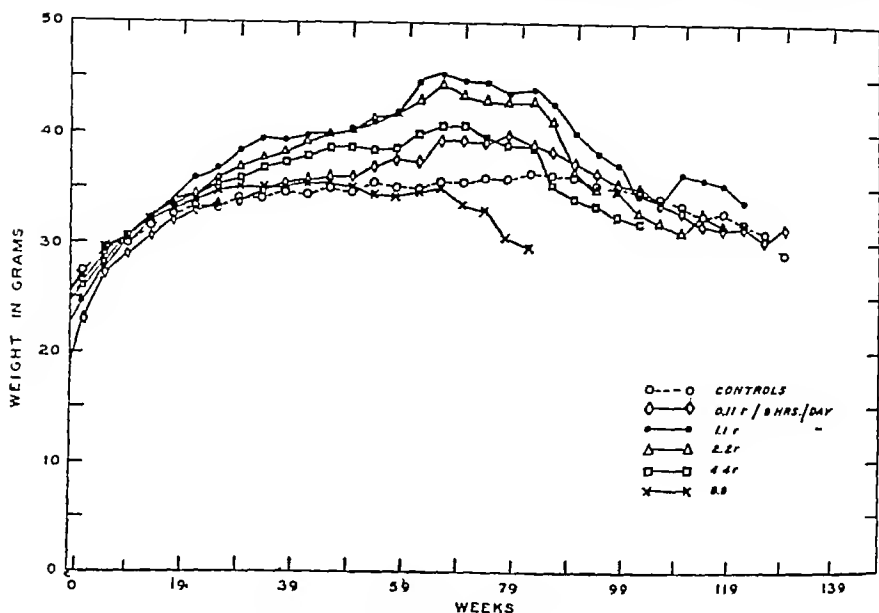


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animals, while in the other groups some of the susceptible ones died from other causes before the disease could manifest itself. The conclusion may be drawn that chronic irradiation does not affect significantly the over-all incidence of cancer but alters only the time at which the tumors appear, indicating a dependence upon dose rate. For a given age, this appears as an increase in incidence with total dose.

A similar picture is presented in the data on the incidence of lung tumors. As lung tumors do not kill mice, however, and may be present for a long time, the over-all incidence as determined in these experiments is merely suggestive. The effect of chronic irradiation upon the incidence of lung tumors was studied in an experiment performed for this specific purpose. Strain A mice, in which the incidence of spontaneous lung tumors is well known (approximately 50 per cent of the animals having lung tumors at the age of twelve months) were exposed to 88 r given in eight hours per day for ten months, to a total dose of approximately 2,500 r. Non-irradiated and irradiated animals of the same age were killed at approximately twelve months of age. It was found that 75 per cent of the irradiated animals showed lung tumors as compared with 50 per cent of the non-irradiated group. This result is statistically significant. Lung tumors in mice are of alveolar origin. The tumors induced by irradiation are microscopically identical with the spontaneous tumors. There is no clear-cut evidence that tumors of bronchogenic origin occur in mice of this strain.

The incidence of mammary carcinoma in LAF₁ mice following long-continued irradiation seems to follow a pattern similar to that for leukemia and lung tumors. Mammary carcinomas are very rare in normal LAF₁ mice, our control series and the 0.11 r series showing a zero incidence. An over-all incidence up to 15 per cent was observed in the groups at the higher dose levels. The genesis of the mammary car-



Fig 8 Subcutaneous sarcoma at the site of a mammary gland in a mouse. Note mammary tissue at right of and above the tumor and the incorporation of mammary ducts in the tumor. $\times 25$

cinomas has been intensively studied. Three causal factors are known: a genetic factor, a hormonal factor, and the milk factor (virus). Speculatively, the occurrence of mammary carcinoma in LAF₁ mice might perhaps be explained in the following manner. The genetic factor is present and hormonal stimulation may be provided as an effect of the radiation on the ovaries. The zero incidence in the control animals may be explained by the existence of a weak milk factor or of an inhibitor. The irradiation may either activate the milk factor or destroy the inhibitor. If we assume the existence of an extra-chromosomal factor and inhibitor in the genesis of leukemia and lung tumors, the results obtained for these tumors might be explained on the same basis.

Mammary carcinomas were found generally in the absence of ovarian tumors. Sarcomas, on the other hand, at the site of the mammary glands (incidence 15 to 25 per cent) were frequently seen in animals with ovarian tumors. Figure 8 shows a subcutaneous sarcoma presumably

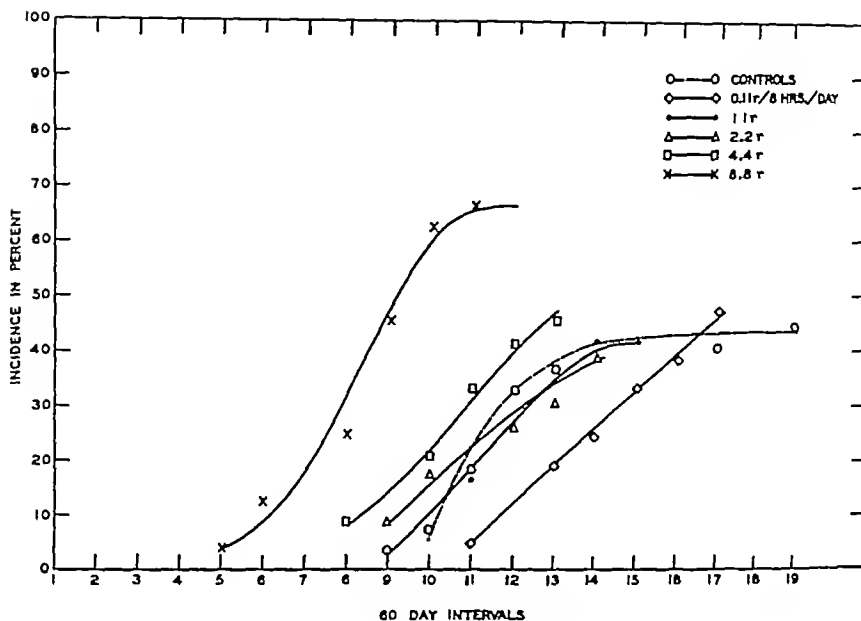


Fig 7 Incidence of leukemia (malignant lymphoma) in female mice (percentage) vs sixty-day intervals

deaths from this syndrome have yet resulted in the animals at the 11 r and 0.11 r level, the maximum dose at the 11 r level being so far approximately 1,500 r. For the three levels of 8.8 r, 4.4 r, and 2.2 r, the total dose seems to govern the occurrence of this terminal condition. Figure 6 gives the death curves from anemia and thrombocytopenia for hybrid guinea-pigs and 2 strains of inbred guinea-pigs exposed to 8.8 r. For the hybrid guinea-pigs the lethal dose extends from 700 r to 4,400 r, while for one of the inbred strains it extends from approximately 1,200 r to 1,600 r, and for the other strain from 1,900 r to 2,100 r. These data illustrate the importance of the use of inbred animals for obtaining reliable quantitative data.

The most important findings in our experiments have to do with the carcinogenic action of long-continued irradiation. While the majority of the tumors occurred in mice, tumors were also observed in guinea-pigs and rabbits, two species in which spontaneous neoplasms are rare. The most important tumors developing in the irradiated LAF₁ mice, which were used for the tumor studies, were leukemia,

lung tumors, ovarian tumors, and tumors of the mammary gland. Tumors of these same types, with the exception of the mammary tumors, were also observed in the non-irradiated control animals.

The leukemia was mainly of the lymphoid cells, myeloid leukemia was rare. Figure 7 shows the incidence of leukemia in the female experimental and control mice. The picture for the male mice is similar, but there is a sex difference in that the incidence in the females is approximately twice as high as in the males. It can be seen from the curves that the time at which the first tumor appears is approximately the same for the animals in the 2.2 r, 11 r, 0.11 r, and control groups. Likewise the over-all incidence is approximately the same in these groups. The 4.4 r group shows a shift toward earlier onset of the disease and this shift is marked in the 8.8 r group. In this group the incidence is approximately 70 per cent. In all other groups it is approximately 45 per cent. The higher incidence for the 8.8 r group may be explained by the fact that the disease appears at a much earlier age so that there was an opportunity for its development in predisposed

animals, while in the other groups some of the susceptible ones died from other causes before the disease could manifest itself. The conclusion may be drawn that chronic irradiation does not affect significantly the over-all incidence of cancer but alters only the time at which the tumors appear, indicating a dependence upon dose rate. For a given age, this appears as an increase in incidence with total dose.

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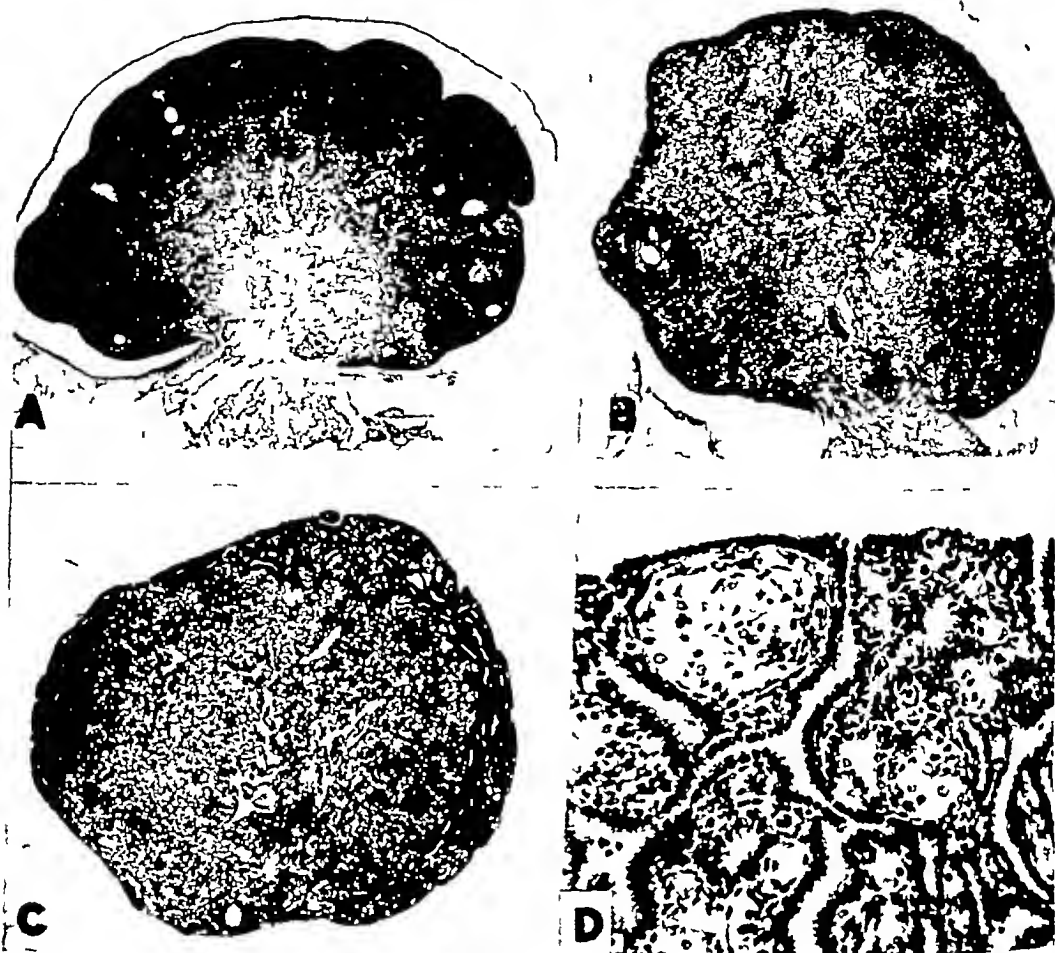


Fig 9 Mouse ovaries stages of degeneration and neoplasia A Normal ovary showing numerous developing follicles $\times 40$ B Disappearance of follicles A single follicle remains and there are no down growths of surface epithelium $\times 40$ C Absence of ova and follicles and beginning proliferation of surface epithelium $\times 40$ D Higher magnification of C showing branching tubular down growths of surface epithelium $\times 220$.

of the mammary gland Note the mammary ducts in the tumor

Ovarian tumors differ in their genesis from the other tumors discussed so far They are the end-product of a degenerative process of the ovary, starting with a depletion of follicles followed by the tubular down-growth of the germinal epithelium and resulting in the formation of three types of growth tubular adenoma, luteal-cell tumor, and granulosa-cell tumor Figure 9 shows this process Figure 10 shows a mixed luteoma and tubular adenoma, while Figure 11 shows a granulosa-cell tumor

Ovarian tumors were observed in only 2 control animals out of 24, at the age of thirty-three and thirty-four months In the different irradiated groups the over-all incidence is 70 per cent to 100 per cent

The role played by radiation in the genesis of these tumors is to hasten the first step, *i e*, the depletion of follicles from the ovaries That subsequent processes are not influenced to any extent by radiation is shown by the fact that on the 88 r level the first tumor was observed at approximately the same age whether the animals received a continuous exposure of 3,500 r or a limited exposure of 880 r

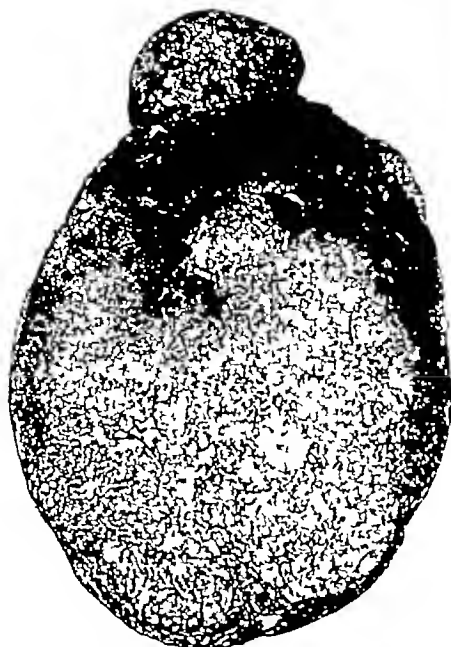


Fig 10 Mouse ovarian tumor, mixed luteoma and tubular adenoma X25 and X225

The induction of these tumors by radiation is not a function of dose rate or total dose, but is dependent upon a minimum dose. This minimum dose is accumulative even in the animals exposed to 0.11 r, which showed a considerably higher as well as an earlier incidence than did the controls, for an accumulated total dose of only 90 r. The first tumor was observed at the age of twenty-eight months, the over-all incidence was 70 per cent. It is also important to note that a single acute dose of 50 r given in four and a half hours at the age of five months will result in an over-all incidence of 70 per cent, the earliest tumor being observed at twenty-three months of age.

A variety of other tumors, such as hepatoma, squamous-cell carcinomas of the vagina and forestomach, and adenoma of the adrenals in males were observed. Their incidence is too low to establish any definite connection with irradiation.

Tumors were also observed in guinea-pigs and rabbits, species in which spontaneous tumors are rare. Of particular interest are several lung tumors in guinea-



Fig 11 Mouse ovarian tumor, granulosa-cell type. X350

pigs following long continued irradiation, for three years or more. All these tumors, so far, have been observed in irradiated animals only. These lung tumors are

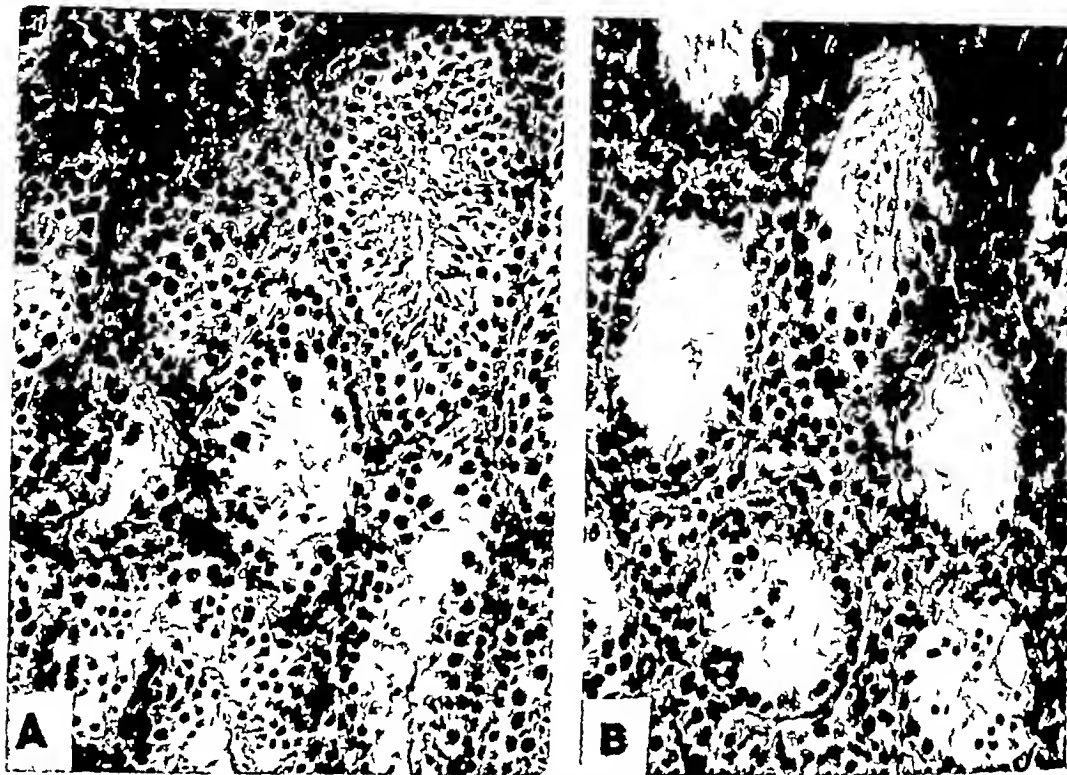


Fig 12 Testes from mice exposed to total doses of approximately 2,500 r whole body gamma irradiation beginning at two months of age. A At the rate of 4.4 r given in eight hours per day. B At the rate of 8.8 r given in eight hours per day. Note the difference in damage to the spermatogenic elements and relative proportions of spermatogenic and interstitial tissue. $\times 225$

presumably of alveolar origin, and their histologic structure is the same as that of lung tumors in mice.

The histologic data as well as the breeding experiments show that radiation injury to the ovary of the mouse is irreversible and cumulative. Radiation injury to the testes of mice and of guinea-pigs, on the other hand, is reversible and cumulative only to a certain degree. Thus LAF₁ males exposed to a total dose of 1,760 r at the 8.8 r level were sterile when mated but regained fertility two months later. In one animal, which was removed from exposure after having received a total dose of 4,700 r, the testes showed normal spermatogenesis when it was killed three months later. The effect of the dose rate is shown in Figure 12. A striking difference in degree of damage of spermatogenic elements is seen in the testes of two animals which were exposed to the same total dose,

approximately 2,500 r, one at the 4.4 r level and one at the 8.8 r level.

Testes of genetically homogeneous mice show little variation in weight for animals of similar body weight and age, and their weight is a sensitive measure of radiation damage. Figure 13 shows dependence of testes weight upon exposure time for three different exposure levels (8.8 r, 4.4 r, and 1.1 r).

After an initial drop, a separate weight level is established for each exposure level, indicating a balance between injury and regeneration. Quantitative histologic studies have shown that the loss of weight is due entirely to a decrease in spermatogenic elements, the amount of interstitial tissue remaining unchanged.

The rapid drop in the weight of the testes of mice in the first few months was used in a study of the intensity effect of chronic irradiation—to determine whether

a daily dose of whole-body irradiation when given over a period of several hours produced the same injury as when given within minutes. For the short-time exposure, 15 minutes, x-rays (170 kv p) were used, and for the long-time exposure, eight hours, gamma rays. The daily dose was 88 r administered six times per week and the total dose 300 r in one experiment and 600 r in another. The weight of the testes of the animals of the long-exposure groups was approximately 50 per cent greater than that of the animals of the

ever, to establish this more conclusively.

The breeding behavior of mice exposed to chronic irradiation and of their offspring completes the picture of radiation damage to gonads and will reveal the induction of genetic changes. Irreversible sterilization effects were observed in LAF₁ female mice following total doses of 770 to 880 r, regardless of the rate and intensity at which the dose was given. The daily doses were 88 r and 44 r given in eight hours or twenty-four hours per day and 55 r given in one hour per day. Lower

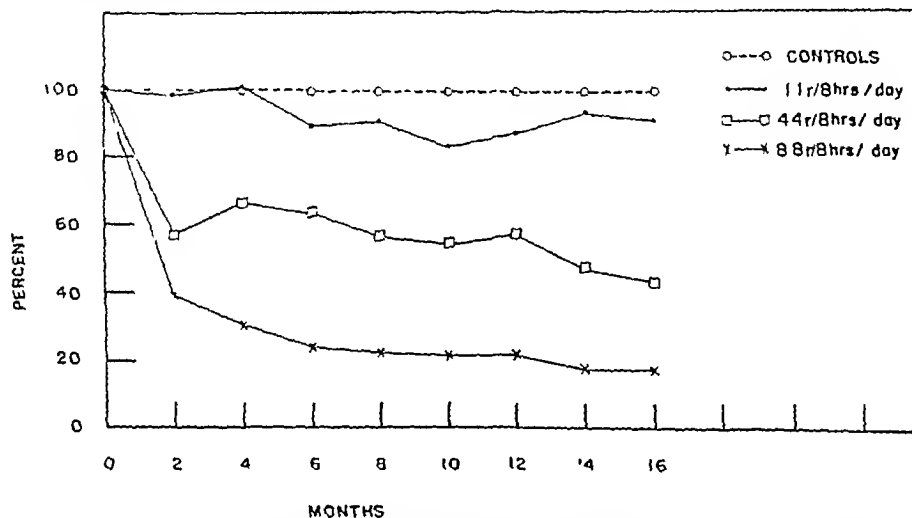


Fig. 13 Effect of long-continued irradiation upon the weight of the testes of mice (percentage of normal)

short-exposure groups. As we do not know whether a biologic quality difference exists between x-rays and gamma rays, the results are merely suggestive. The same effect, however, was found in an experiment just completed in which only x-rays were used. Two groups of mice were given a daily dose of 10 r, five times per week, to a total dose of 300 r. One group received the exposure in 137 minutes and the other in 4 hours and 186 minutes. The intensity difference was obtained by keeping tube voltage (170 kv p) and current (20 ma) constant and changing filtration and focus-animal distance. It seems, therefore, that an intensity effect in long-continued irradiation exists so far as the mouse testes are concerned. Additional experiments, are necessary how-

dose rates could not be used, as the period of fertility of mice is only eight months. Radiation effects consisted in sterility in some animals and production of litters of reduced size in others. Very few of the animals bred a second time.

Male LAF₁ mice, when exposed to a total dose of 1,100 r at the 88 r level, and then removed from the field, bred with reduced first litters and later normal litters. When exposed to 1,760 r at the same level, they were sterile but began to breed normally after two months. Male mice exposed to 1,100 r at the 44 r level bred normally.

In less vigorous inbred strains, as C3H and dba, irreversible sterilization of the females was observed following doses of approximately 450 r at the 44 r level,

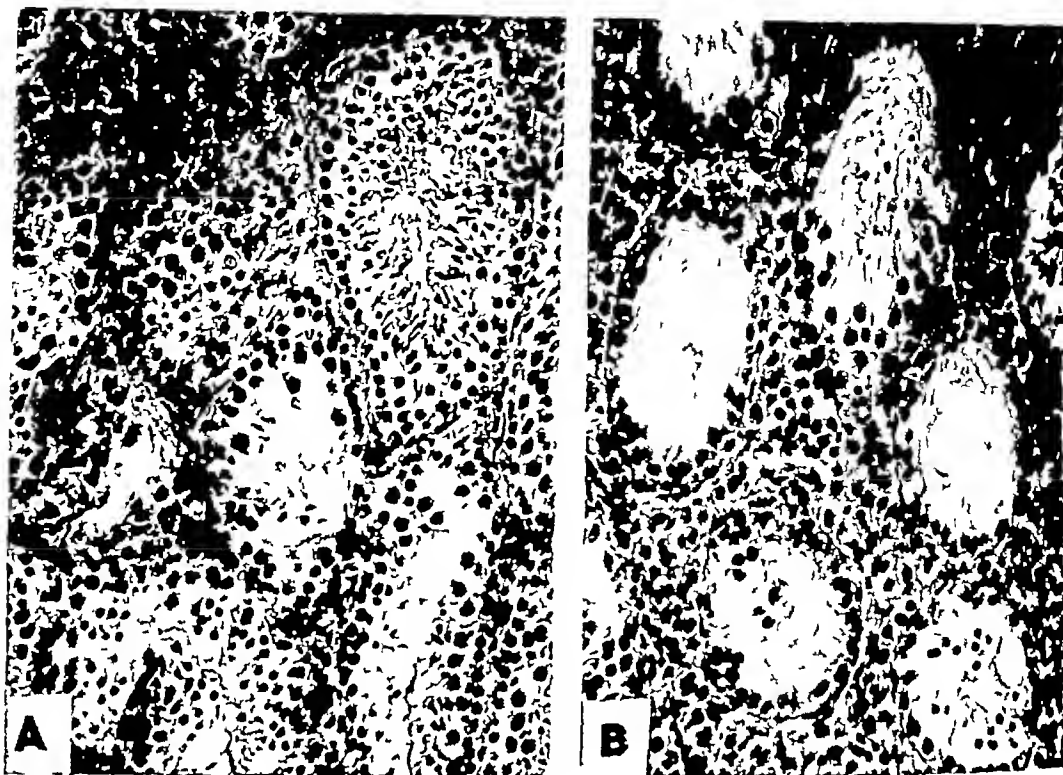


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The rapid drop in the weight of the testes of mice in the first few months was used in a study of the intensity effect of chronic irradiation—to determine whether

more than the permissible dose of 0.1 r. Since our data show no radiation injury to the skin of experimental animals exposed to 8.8 r given in eight hours per day to total doses up to 10,000 r, it seems possible to increase the permissible dose to hands to 1 r per day.

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SUMARIO

Estudios Biológicos en la Escala de Tolerancia

Ratones de tres razas insitas, cobayos y conejos fueron expuestos a prolongada radiación gamma a dosis diarias que variaron de 0.11 a 8.8 r, administradas ya ocho o veinticuatro horas al día. Los experimentos revelaron que la prolongada absorción de rayos penetrantes va acompañada de lesiones aun a la dosis mínima (0.11 r) administrada ocho horas diarias.

El cuadro sanguíneo no ayudó mayor cosa a determinar las lesiones vinculadas con la radiación. La carcinogénesis y la esterilidad constituyeron las características sobresalientes en la patología debida a la radiación. En los tumores ováricos la dosis oncogénica resultó ser acumulativa e independiente de la magnitud de la dosis

diaria, por lo cual debe mantenerse la actual dosis "tolerable" de 0.1 r al día, reduciéndola quizás en las mujeres a 0.02 r al día, a menos que se acorte el período de exposición.

En lo relativo a alteraciones genéticas, la actual dosis "tolerable" parece proporcionar un margen suficiente de seguridad al efecto de que no sobrevendrá un aumento descubrible en el coeficiente de mutaciones y translocaciones de genes.

Los datos obtenidos indicaron, además, la intervención de un posible factor de intensidad, por lo cual deben evitarse las exposiciones diarias y muy cortas durante períodos prolongados.



while male mice became sterile following a total dose of 800 r at the same level.

No conclusive evidence for the production of genetic changes was obtained in LAF₁ mice receiving the chronic exposures in our experiments, nor in those C3H and dba mice which were exposed continuously up to six generations to 1 l r given in twenty-four hours per day after fertilization of the ova. Likewise no evidence for the production of translocations was obtained in offspring of male LAF₁ mice exposed to 88 r given in eight hours per day to a total dose of 1,100 r and in the offspring of female mice exposed to 88 r given twenty-four hours per day to a total dose of 770 r. Approximately 12,000 mice were used in these studies. This is in contrast to observations of hereditary change in the offspring of mice given acute exposures. Since the work of Snell (1) indicates that hereditary changes are more likely to be observed as a result of irradiation of mature sperm and ova, the failure to find such changes following chronic exposure may be due to the comparatively low total dose received by the mature sex cells.

Beside the effects of chronic irradiation which have been discussed, there were few changes observed in other tissues and organs. No graying or loss of hair or atrophy of the skin was seen in any of the three species up to the highest doses. There was no opacity of the eyes, no pneumonitis or changes in the gastro-intestinal tract. This is quite in contrast to observations on acute exposures.

What conclusions can be drawn from these data with regard to the problem of human protection against penetrating radiation? It is obvious that as long as no data are available on man, we have to be guided by findings in experimental animals. As the experiments have shown that long-continued absorption of penetrating radiation is associated with damage even for doses of 0.11 r given in eight hours per day, we may define a permissible dose for chronic irradiation as one in which the damage cannot be expressed in patho-

logical changes. The damage may express itself in a possibly unimportant shortening of the life span.

The experiments indicate that the blood picture is of little value in determining radiation damage, except in case of obvious over-exposure. We have seen that carcinogenic action and sterility effects dominate the picture of radiation injury. Mice and guinea-pigs exposed to 1 l r show an essentially normal blood picture for total accumulated doses of over 1,000 r, yet an appreciable decrease in life span and an increase in tumor incidence occur in mice. We know, at least in the case of the ovarian tumors, that the tumor-inducing dose is cumulative and independent of dose level.

Hence, it is of paramount importance that the present permissible dose of 0.1 r per day be maintained. Human ovaries are somewhat less radiosensitive than mouse ovaries according to Peck and collaborators (2), approximately 700 r in divided doses are necessary for permanent sterilization, while a single whole body exposure of 300 r to LAF₁ mice produces sterility. As ovarian tumors in mice are similar in type to those observed in human beings, we may have to assume, unless shown otherwise, that in the latter similar degenerative processes may be induced by chronic irradiation and lead to tumor formation. It follows that the permissible dose of 0.1 r per day should be reduced for women to perhaps 0.02 r per day or that the time of exposure should be reduced to a few years.

As far as genetic changes are concerned, our data indicate that the present permissible dose gives a sufficiently wide margin of safety that a detectable increase in rate of gene mutations and translocations will not occur.

Our data also suggest that an intensity factor exists. Daily exposures of very short duration over long periods of time should therefore be avoided.

In certain types of work, *e.g.*, handling of radioactive substances, a larger permissible dose to the hands may be considered safe if the rest of the body does not receive

other factors, were largely disregarded or the radiation employed was not actually "penetrating"

Because our knowledge of the biological effects of radiations in general and of certain radiations and radioactive materials specifically was so superficial, the medical and biological divisions of the Plutonium Project were organized. The objectives of the Health Division were essentially to study the fundamental and comparative action of radiations and radioactive materials and to apply the findings to the protection of personnel who worked with, and the public which was potentially in danger of exposure to, these physical hazards.

The extensive studies on the biological effects of acute and chronic externally originating whole-body irradiation, as well as internally deposited radioactive isotopes, are reported in detail in the volumes of the Plutonium Project Record. In this report consideration is given only to selected aspects of the subject.

EFFECTS ON ANIMALS OF WHOLE-BODY CHRONIC EXPOSURE TO EXTERNALLY ORIGINATING RADIATIONS

The problem about which we knew least before the war and which was of great importance to us from a practical standpoint was the effect of chronic daily whole-body exposure to ionizing radiations originating outside the body. In particular, we were in need of data on the biological effect of chronic irradiation in the region of the "tolerance dose." Our problems, so far as "whole-body" externally originating radiation was concerned, had to do chiefly with gamma rays, x-rays, beta rays, and neutrons.

The problem of exposure of the external surface of the body to beta rays was a special one because of the relatively short penetration of these rays in tissue. This problem has been explored by Raper and Zirkle (15, a, b) and others (16). Experiments involving the chronic exposure of animals (mice) to fast neutrons have also been carried out by Zirkle, Raper *et al* (17). The only experiments, however, in which

the peripheral blood was studied in an adequate number of animals, with reliable frequency, to be of interest in this presentation, have been those confined to x-ray and gamma ray exposure.

Zirkle and his co-workers in planning their chronic exposure experiments with neutrons chose dosages which, on the basis of the γ/n ratio already established by their previous work (18, 19) were in the neighborhood of the "tolerance range" and above. In addition, chronic gamma ray exposures in the Clinton pile were carried on simultaneously for comparative purposes (20). Chronic exposure of rats to small daily doses of x-rays has been carried out at the University of Chicago (21), and of mice at the National Cancer Institute (22). In these experiments the exposure of the animals was for only relatively short periods (minutes) and, therefore, is not strictly comparable to the type of exposure sustained by personnel who were working with radiations and radioactive material in the laboratory eight hours, six days per week. With this in mind, Lorenz *et al* (23) designed an exhaustive experiment which would largely duplicate in animals the laboratory exposure which scientists and their assistants might sustain in radiation laboratories. The species studied were rabbits, mice, and guinea-pigs. Blood studies covered erythrocytes, hemoglobin, leukocytes, the differential leukocyte count, platelets, reticulocytes, and in special instances erythrocyte diameter. Control blood counts were made on the animals at least twice before placing them in cages arranged in a circular manner about a large centrally placed radium source. The geometric arrangement was such that the animals in the cages placed in fixed positions received definite exposures deliberately planned.

Two groups of guinea-pigs were used in this study. One group was from a heterogeneous National Cancer Institute stock and the other was a special hybrid group. The rabbits were regular National Cancer Institute stock and the mice were of two strains: a special LAF₁ strain which was selected because of resistance to the com-

The Hematological Effects of Ionizing Radiations in the Tolerance Range¹

LEON O. JACOBSON, M.D., and E. K. MARKS

University of Chicago

THE INADEQUACY of the experimental and clinical data upon which the "tolerance dose" of various ionizing radiations is based became quite apparent to those of us charged with the responsibility of protecting the personnel working on the atomic bomb project from "over-exposure" to these agents. It was also apparent that no clinically applicable tests were known which would detect biological alterations in an animal or human being exposed to doses of radiation in the "tolerance range."

Many facts were known regarding the biological effects of ionizing radiation before the war. The adverse effects of radiations upon the blood-forming tissue and the reflection of such effects in the peripheral blood were recognized with the pioneer work of Heineke in 1903 (1). Innumerable investigators had studied other biological and clinical effects. The purely experimental data available, however, were confined largely to animal studies in which lethal or near-lethal doses of externally applied roentgen and gamma rays or fast neutrons were given either to a part or to the whole body in one (acute) dose or in closely spaced divided doses. The purely clinical data were limited to reports on the effects of therapeutic doses of these same radiations given to local areas of the body and in relatively large single or divided doses. No deliberate studies in animals or man had been reported in which chronic exposure to ionizing radiations was within the "threshold" or "tolerance range." A few reports available from clinics and from radium institutes indicated that as far as whole-body chronic exposure was concerned, the

hematologic constituents of the peripheral blood were the most sensitive indicators of radiation effect (2, 3). These reports dealt exclusively with professional and non professional personnel concerned with the preparation of radium sources and the administration of radiations for therapeutic purposes. The amount of exposure such workers received over extended periods, however, was in most cases largely estimated rather than accurately measured.

The information available on the biological effects of radioactive isotopes deposited within the body was derived chiefly from the radium-dial industry and from the more recent therapeutic and tracer studies with the relatively short-lived isotopes such as P^{32} (4), Sr^{89} (5), I^{131} (6), and Na^{24} (7). Reports on the radium-dial painters described patients with terminal anemia, radiation osteitis, and osteogenic sarcoma, but the accumulated initial doses of radium were unknown and only the residual deposition was ascertainable (8a, b). The tracer and therapeutic studies with "short-lived" artificially produced radioactive isotopes were not directed toward the study of the more general biologic effects. Some experimental work had been done, however, with radium (9, 10).

Statements are abundant in the literature stressing the significance of a lymphocytosis (11), a monocytosis (12), an eosinophilia (13), or a leukopenia (14) in the peripheral blood as an indication of the effects of chronic radiation exposure. Many of these reports are confined to poorly controlled human studies or animal experiments in which the individual variations and/or numbers of subjects, as well as

¹ The work reported herein was done in the Metallurgical Laboratory, University of Chicago, under the Manhattan Project. This paper is a brief version of material to be published in the Plutonium Project Record of the Manhattan Project Technical Series. Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

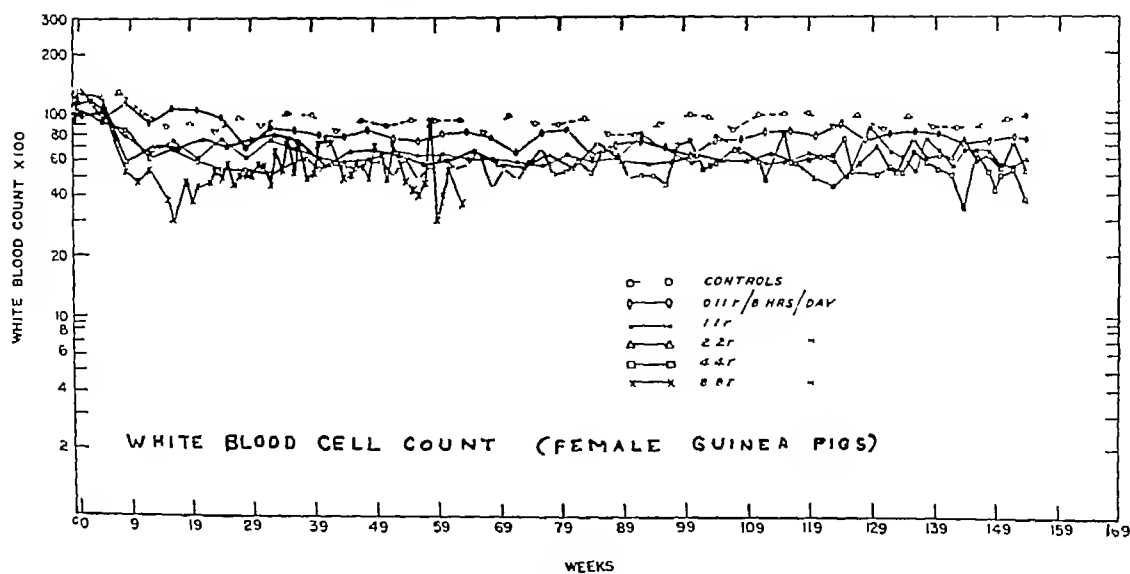


Fig 2 Effect of chronic gamma ray (radium) exposure on the white blood cell values of the peripheral blood of female guinea pigs

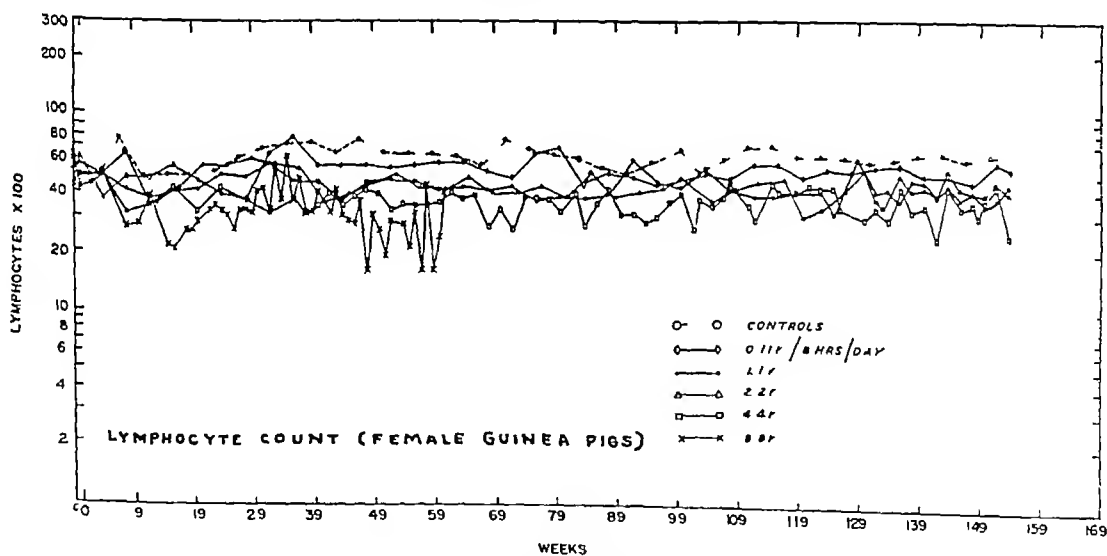


Fig 3 Effect of chronic gamma ray (radium) exposure on the lymphocyte values of the peripheral blood of female guinea-pigs

duction in other hematological values showed no histologic evidence of abnormality of the blood-forming tissues

5 The acute onset of a severe anemia was a common cause of death of guinea-pigs exposed on the 8.8 and 4.4 r exposure level. A similar observation was made in chronic radium toxicity in dial painters and has been observed also in animals exposed to γ -rays (24), neutrons (25), and such radioactive materials as plutonium (26 a),

radium (26 b), strontium (26 c), phosphorus (27), and others. The mechanism of this phenomenon is poorly understood.

6 Macrocytic anemias appeared in certain animals on chronic exposure to doses in the range under discussion. The etiology of this anemia is obscure at the present time. That it is not due to direct irradiation of gastro-intestinal tissues is brought out by the fact that it may be produced also by radioactive isotopes which

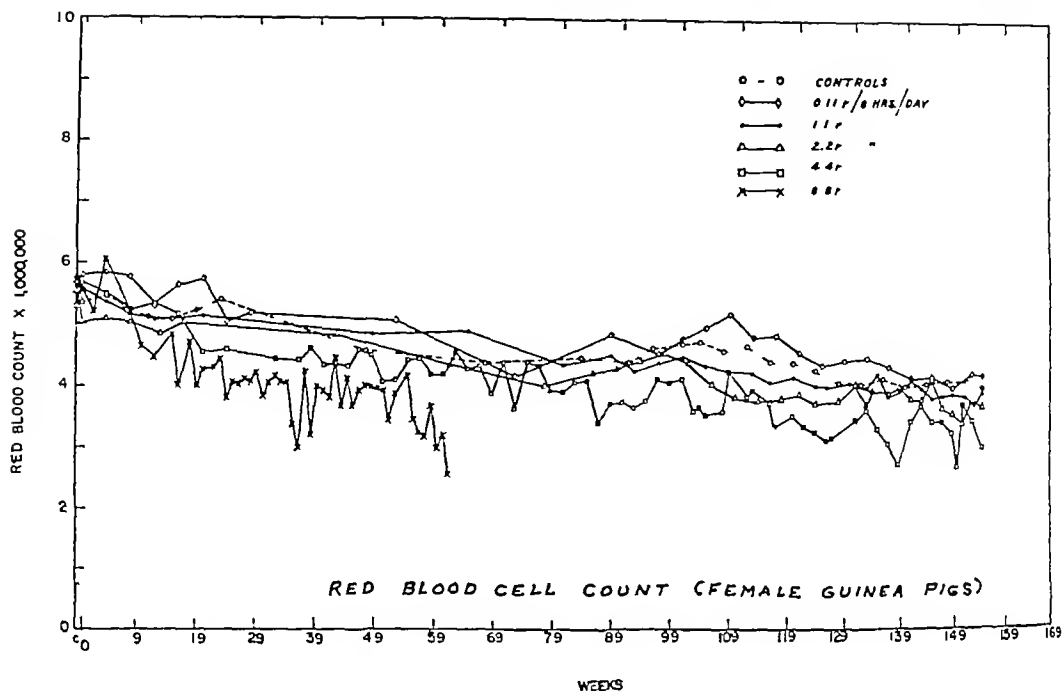


Fig 1 Effect of chronic gamma ray (radium) exposure on the red blood cell values of the peripheral blood of female guinea-pigs

mon "mouse typhoid" and pneumonia and because of a low spontaneous tumor incidence, and the A strain which normally has a high incidence of lung tumors

The species and substrains of laboratory animals were divided into groups and exposed to doses of 0.1, 1.1, 2.2, 4.4, and 8.8 r, some for eight hours per day and others for twenty-four hours per day, six days weekly. The animals were observed while thus exposed over periods now extending well beyond three years. Neither were significant effects on the hemopoietic tissues noted nor were significant effects reflected in the peripheral blood in any of these species chronically exposed to 0.1 r per day for three years or more. The guinea-pigs receiving a 1.1 r daily exposure showed an equivocal reduction in the number of lymphocytes, but in rabbits and mice no change in the hematological constituents of the peripheral blood was noted with this dose even after three years or more of daily exposure. With doses of 2.2, 4.4, and 8.8 r daily, however, significant hematological changes were eventually apparent in all three species. The severity of these ef-

fects varied with the species, guinea-pigs were most sensitive, mice intermediate, and rabbits relatively resistant. Figures 1-7 illustrate the effects on the peripheral blood of these animals.

Certain extremely significant aspects of these experiments should be emphasized.

1 In female mice certain biological effects appear in the absence of detectable hematological changes. Ovarian tumors developed in mice exposed to 0.1 r per day and 1.1 r per day, while no changes in the peripheral blood were detectable at any time during the three years of exposure to these doses.

2 No lymphocytosis, eosinophilia, or monocytosis, findings commonly believed to indicate chronic radiation damage, occurred in any of the three species exposed chronically to doses between 0.1 and 8.8 r per eight-hour or twenty-four-hour day.

3 Lymphocyte reduction was the earliest abnormality noted in the peripheral blood of these three species after chronic exposure.

4 Animals which developed a lymphopenia or, indeed, a moderate insidious re-

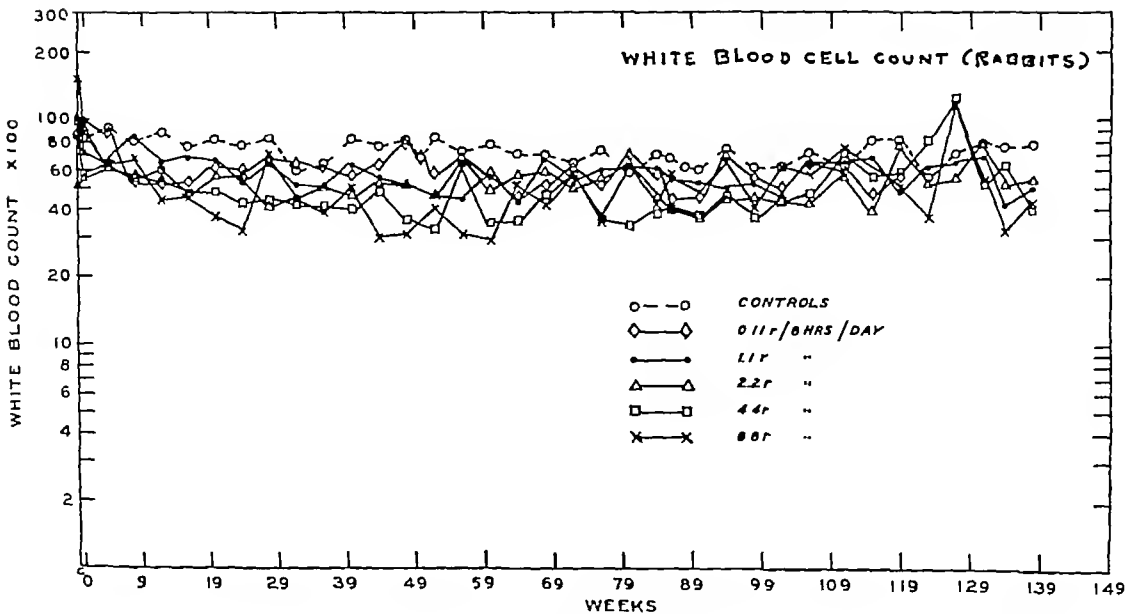


Fig 6 Effect of chronic gamma ray (radium) exposure on the white blood cell values of the peripheral blood of rabbits

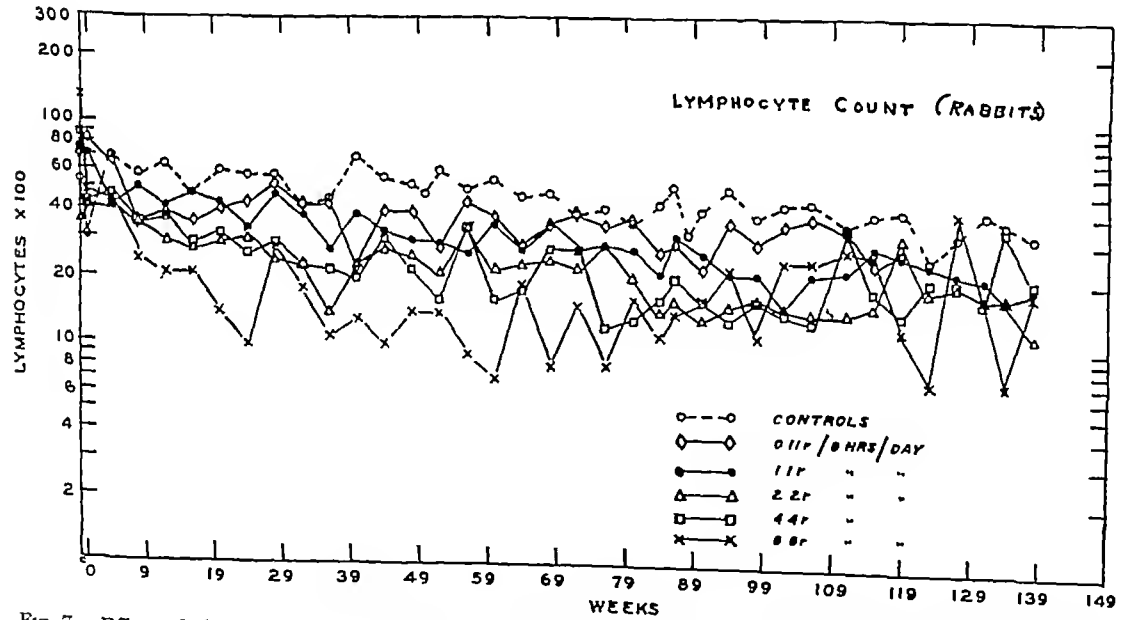


Fig 7 Effect of chronic gamma ray (radium) exposure on the lymphocyte values of the peripheral blood of rabbits

ministered in divided daily doses of 5 to 20 r. The daily treatment in each case required only a relatively few minutes of exposure. A case of polycythemia rubra vera treated in this manner illustrates the degree of effect which may occur with an exposure of this magnitude (Fig 8). In general, these studies indicate a sensitivity of

the hemopoietic system of man comparable to that of the guinea-pig and dog. With accumulated doses of 300 r (skin surface dose) leukopenia, and particularly lymphopenia, occurred. The severity of this reaction varied widely from individual to individual. A striking effect was the definite macrocytic anemia which developed in

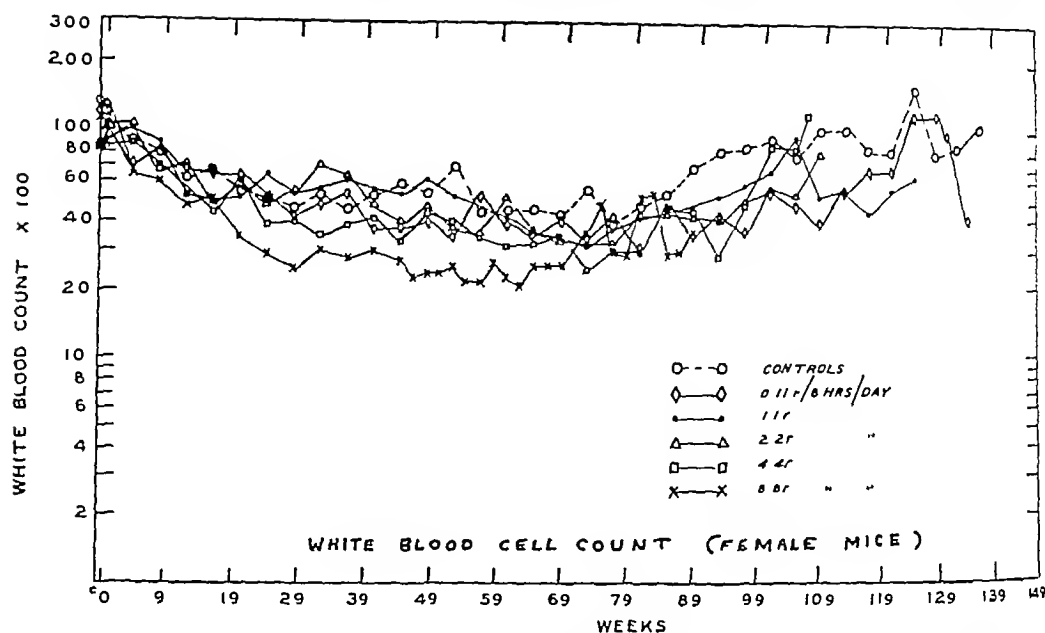


Fig 4 Effect of chronic gamma ray (radium) exposure on the white blood cell values of the peripheral blood of female mice

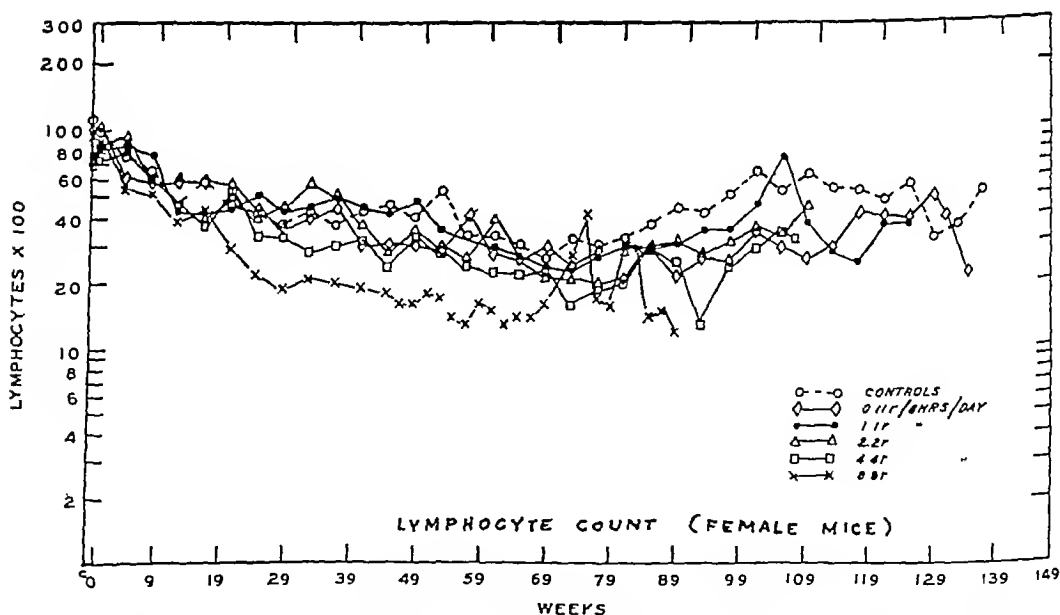


Fig 5 Effect of chronic gamma ray (radium) exposure on the lymphocyte values of the peripheral blood of female mice

localize in blood-forming tissue and spare the digestive tract (26, a, b, c)

CHRONIC EXPOSURE OF MAN IN THE "TOLERANCE RANGE"

The studies of Low-Beer and Stone (28),

Craver (29), and Nickson, Cantril, and Jacobson (30), in which human beings have been exposed to whole body roentgen irradiation in divided doses are of interest. Total doses up to slightly more than 300 r (in air at the body surface) have been ad-

changes in the blood or blood-forming tissue. However, it usually requires an autopsy to find these pathological alterations and we lack a practical means of discovering such incipient changes. The dose of radioactive isotopes required to produce bone sarcomas, lymphomas, and the like in animals is practically identical with that required to produce perceptible effects in the peripheral blood.

CONTROLLED STUDIES OF PERIPHERAL BLOOD OF PROJECT PERSONNEL EXPOSED OR POTENTIALLY EXPOSED TO RADIATIONS

An extensive study of the hematological constituents of the peripheral blood of Plutonium Project personnel was undertaken at the inception of the program and still continues. This was done in an attempt to discover evidence of incipient damage from radiation exposure. We were aware of the fact that significant biological effects resulting from exposure to these agents, which could be detected by clinical laboratory examination, invariably meant that serious damage had already occurred. Prophylactic measures designed to prevent or minimize the danger of irreversible damage to the health of Project personnel from these physical agents were therefore considered paramount.

All persons accepted for employment and placed in a particular job or position were classified in terms of individual occupational hazard in one of two groups: (1) the control group and (2) the work-hazard group. This division was not made in terms of the usual understanding of occupational hazards but rather in terms of the radiation hazards peculiar to the Plutonium Project.

The control group consisted of all employees working in areas in which exposure to radiations was negligible or absent. The work-hazard group consisted of all those laboratory workers who were exposed or potentially exposed to physically hazardous materials. The frequency of the hematological observations in these two groups varied from daily studies to studies conducted every three months.

The number and variety of hematological abnormalities found during a typical month of operation at the Metallurgical Laboratory in Chicago were great. Proper evaluation of these abnormalities posed a serious clinical problem, since the part played by the work hazard needed an answer in each individual case. For example, if a leukocyte count was found to be below 3,000 per cubic millimeter, it was immediately checked by calling the individual back to the clinical laboratory for a second count. The problem was to determine whether the abnormality was secondary to a coincidental infection, or of other origin, or was actually related to the physical hazard entailed in working with a radiation source or sources. Occasionally the individual was of necessity subjected to careful questioning concerning his work activity and his present health, and a physical examination was frequently necessary. The room or rooms in which he was working were investigated by the health physicist and frequently the previous week or weeks of activity were reconstructed with the help of the individual's immediate supervisor in order to ascertain as nearly as possible the amount of radiation exposure involved. When "film badges" and "ionization chambers" became available in sufficient quantity and were worn by workers, the approximate amount of external radiation accumulated by an individual for any period was known. Such records obviously made a decision as to the part played by radiation in causing leukopenia much simpler.

The need for careful interrogation and physical examination of personnel in whom leukopenia developed is illustrated by the following account of one of many related incidents. Certain research groups working intimately with large radiation sources, such as fission products, or in the vicinity of an experimental "pile" had hematological studies at frequent intervals, once to twice weekly in certain cases. This seemed indicated, since it was not unlikely that large acute exposures would be sustained. Several individuals in one such group were

many of those exposed to total doses of this magnitude. Spontaneous recovery of the hematological constituents of the peripheral blood of these individuals was universal, but the time required for recovery varied widely.

logical picture, depend on the size of the administered dose and the extent of localization within this particular tissue. With all radio isotopes which we have studied thus far, whether they were localized to bone or more generally distributed in the

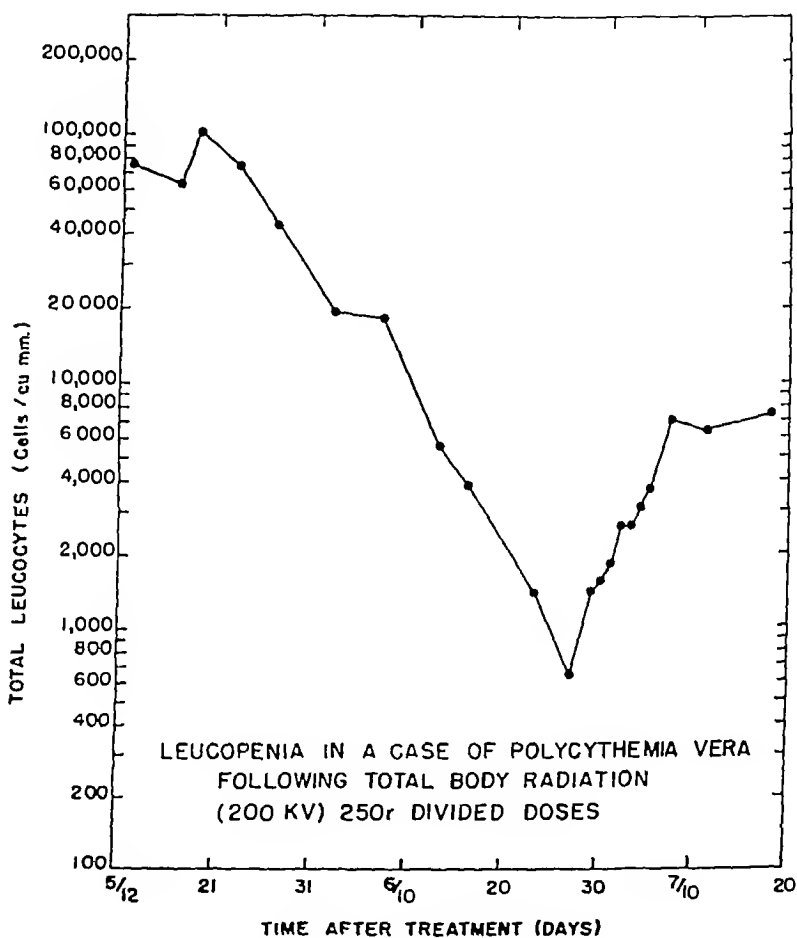


Fig 8 Polycythemia rubra vera exposed to whole body irradiation in divided doses

COMPARATIVE EFFECTS OF PARENTERALLY AND EXTERNALLY ADMINISTERED RADIOACTIVE ISOTOPES (Acute and Chronic Studies)

The studies of Brues *et al* (31), Bloom *et al* (32), Jacobson *et al* (33, 26 a, b, c,) cover the general biological effects of the radioactive isotopes on animals. So far as the peripheral blood is concerned, the severity and the rapidity of the effect on blood-forming tissue of the fission products, and its consequent reflection in the hemato-

body, a reduction in the lymphocyte values of the peripheral blood is the most sensitive indicator of acute or subacute effect. Lymphocyte reduction may occur even in the absence of histologic evidence of effect on lymphatic tissue. This is perhaps of practical importance and is also true of animals chronically exposed to externally originating radiation (gamma and roentgen rays). On the other hand, histopathologic changes in organs and tissue may occur in the absence of or prior to observable

hour to hour, day to day, and month to month made it almost impossible to interpret minor fluctuations which may have resulted from acute or chronic radiation exposure

SUMMARY AND CONCLUSIONS

Prior to the second world war the clinical and experimental data which were available on the biological effects of various ionizing radiations in the "tolerance"² or "permissible" range were inadequate. The literature emphasized the usefulness of hematological studies of the peripheral blood of man and animals exposed to these radiations for the detection of early radiation injury.

Studies conducted on the Plutonium Project with experimental animals and human beings indicate that

(1) Lymphocyte reduction in the peripheral blood is the most sensitive indicator of acute or subacute exposure to externally originating ionizing radiation or internally deposited radioisotopes

(2) No hematological change is detectable in the peripheral blood in mice, rabbits, or guinea-pigs with a daily whole body exposure to 0.1 r of gamma radiation extending over three years. In mice chronically exposed to a dose of this magnitude, however, ovarian tumors develop.

(3) Guinea-pigs show an equivocal reduction in lymphocyte values after chronic daily whole body exposure to 1.1 r per day. Rabbits, mice, and guinea-pigs exposed to doses of 2.2, 4.4, or 8.8 r show definite hematological changes of significance after varying lengths of time. The guinea-pig is the most sensitive, the mouse intermediate, and the rabbit most resistant so far as hematological changes produced by radiations are concerned.

(4) Human beings subjected to whole body x-ray exposure totaling 300 r (skin dose) given in divided daily doses of 5 to 20 r showed a degree of sensitivity of the hemopoietic system roughly comparable to that of the guinea-pig and the dog.

² Tolerance = 0.1 r per day as set by the National Bureau of Standards

(5) In studies conducted on Plutonium Project personnel no hematological changes occurred which were referable to radiation exposure in the "tolerance range."

(6) Clinically applicable tests to determine and evaluate incipient damage to personnel from radiation exposure in the "tolerance range" are urgently needed. Reliance on studies of the hematological constituents of peripheral blood is dangerous, since no findings can be expected with exposure in this range. The appearance of hematological changes in personnel working in the field of nuclear physics or medicine, which are referable to an acute or chronic exposure to radiations, should be interpreted as serious and probably should preclude further actual or potential exposure of the worker thus affected.

Department of Medicine

University of Chicago

Chicago 37, Ill

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found to have leukocyte counts of less than 3,500 on one particular examination, their previous counts having been 5,000 or over. Immediate investigation indicated that they probably had early German measles and subsequent observation proved this to be true. In other instances it was not possible to relate leukopenias to infection or indeed to any ascertainable cause. Even if the survey of the work area for possible radiation exposure indicated essentially insignificant findings, the question of chance overexposure due to carelessness or utter disregard of caution on the part of the individual had to be considered. If it seemed warranted, the worker was removed from all possible chance of radiation exposure and observed carefully from the hematological and clinical standpoint. The practice of shifting workers from areas of high or potentially high radiation exposure to areas in which exposure was negligible was not uncommon if laboratory findings warranted caution.

Special studies were conducted on individuals who had developed a leukopenia.

1 Thirty-five persons with leukocyte counts from 4,800 to 3,150 per cubic millimeter were subjected to the "standing running exercise" for one minute, during which time they exerted themselves to the utmost and raised the feet above the floor at least 12 inches. Individuals with normal leukocyte values were subjected to the same test for comparative purposes. In every instance, an increase in the leukocyte value occurred immediately after exercise. No correlation existed between the type of response to the "exercise test" and degree of exposure to radiation.

2 Leukocyte and differential counts were made on a number of individuals showing leukopenia at 8 30 A M, 11 00 A M, and 4 00 P M, of the same day. Seventy-five per cent showed an increase in the white cell count at the 4 00 P M determination, 16.6 per cent remained essentially the same, and 11.9 per cent showed a slight further decrease. Forty per cent of the leukocyte counts remained essentially unchanged at the 11 00

A M determination, 25 per cent were slightly decreased, and 35 per cent were slightly increased. No particular value of a practical nature could be assigned to these results except that a relatively normal diurnal fluctuation was obtained. The fact that certain individuals failed to respond with an increased, decreased, or unchanged leukocyte value could not be correlated with an increased exposure to ionizing radiation.

3 The effect of the injection of adrenalin into individuals with leukopenia was compared to its effect in individuals with normal leukocyte counts. Again the response was comparable in those with leukopenia who were exposed to radiation and in those with leukopenia with no such exposure.

4 Sternal bone marrow aspiration studies were made in cases of persistent leukopenia. No abnormalities were encountered.

5 Morphological studies on the erythrocyte and nucleated constituents of the peripheral blood conducted on control and work-hazard groups failed to indicate changes attributable to radiation exposure. Cooke and Ponder's modification of the Arneeth count (34) was used to determine whether a shift in the maturation of the polymorphonuclear cells in laboratory personnel had occurred as a result of exposure to radiations. No evidence of a positive nature was obtained. The total lobe count of work-hazard personnel varied little from that of personnel from the control group.

On the Plutonium Project relatively few instances were encountered in which changes in the hematological constituents of the peripheral blood of personnel could be definitely attributed to contact with external radiation or the deposition of radioactive materials within the body. The great variation in the steady state of the various hematological constituents of the peripheral blood from one individual to another, the inaccuracy of modern methods for measuring these constituents, and the individual physiological variation from

hour to hour, day to day, and month to month made it almost impossible to interpret minor fluctuations which may have resulted from acute or chronic radiation exposure

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Leon O Jacobson, MD (Chicago Ill) As the newspapers of the country pointed out, there were some fatal accidents at Los Alamos, and other people who were exposed showed effects comparable to those which have been illustrated in the course of this Symposium. I would have preferred to have Dr Hempleman say something about these accidents rather than to talk about a matter with which I had very little to do. We

saw a couple of the men after they returned to Chicago, so I do know that they had changes in the peripheral blood, but I did not see either of the fatal cases

So far as recovery is concerned, Dr Lorenz has an experiment which is now in progress. I believe that it deals directly with this problem.

Egon Lorenz, Ph.D. (Bethesda, Md.) The experiments which Dr Jacobson has spoken about consisted in exposing inbred guinea-pigs to 88 r (gamma rays) given in eight hours per day to such a total dose—approximately 1,000 r—that the erythrocyte count dropped to approximately 2,500,000, with a corresponding drop in leukocyte and platelet counts. These guinea-pigs were then removed from the exposure field. In all of them the erythrocyte count continued to drop, sometimes to values of one million. Approximately 50 per cent of the animals died of aplastic anemia, the others recovered slowly and, after several months, the blood picture approached normal values with erythrocyte counts near 4,000,000, which is slightly below that of non-irradiated guinea-pigs of the same age.

In some of the animals which survived, with a return of the blood picture to almost normal values, anemia and thrombocytopenia again developed and death occurred within a few weeks. For the present we have no explanation for this second drop in erythrocyte and platelet counts.

Robert S. Stone, M.D. (San Francisco, California) Doctor Jacobson asked if I would comment on some experiments that Dr Low-Beer and I have been conducting at the University of California Hospital since 1942. We have been treating patients suffering from rheumatoid arthritis, degenerative arthritis, and metastatic carcinoma, with total body irradiation. These patients had relatively normal blood pictures at the start and their blood pictures have been followed for periods up to four years after the irradiation. Our observations would lead us to believe that just as the human skin never wholly recovers from even minor damage caused by x rays, so the hemopoietic tissue never completely recovers.

The length of time one takes on vacation, or away from radiation, represents just so much time during which one is not being exposed. Whether such time contributes materially to recovery from radiation effects is not established. Possibly Dr Bloom may throw some light on the problem of recovery. Dr Low-Beer's results, when published, will show that effects can be detected 100, 200, and even 300 days after treatments are finished. In so far as effects on the red blood cell count and hemoglobin content of the peripheral blood are concerned, the maximum effect is not seen for 200 or 300 days. Such late manifestations convince me that there is some permanent derangement that we ordinarily do not detect. We must think of all radiation effects as being at least partially permanent effects.

By taking one month a year as vacation from exposure to ionizing radiations, one lessens one's exposure per year by one twelfth, but one can be sure that he does not by such a rest period fully recover from such damage as may have occurred during the preceding year. The only method of being absolutely sure of not having effects is to protect oneself adequately at all times.

Before closing, let me emphasize what Dr Hodges has said. When we of the Plutonium Project speak of damage, or lack of it, to personnel, we are referring only to that part of the Atom Bomb Project for which we were responsible. As is explained in the Smythe report, the "Metallurgical" or Plutonium Project centered around the University of Chicago in Chicago, the Clinton Laboratories in Oak Ridge, Tenn., and the Hanford Engineers Works near Richland, Wash. It was concerned with making chain-reacting piles to produce plutonium, producing plutonium, and separating it from uranium and fission products. Hence the Health Division was concerned with great radiation problems. Other parts of the "Manhattan Project" had their own problems and their own health organizations, for which we had no responsibility and over which we exercised no control.

SUMARIO

Efectos Hematológicos de las Radiaciones Yonizantes en la Escala de Tolerancia

Los estudios efectuados en el Proyecto del Plutonio en animales de experimentación y seres humanos indican que

(1) La linfopenia en la circulación periférica constituye el índice más delicado de

la exposición aguda o subaguda a la radiación yonizante exógena o a radioisótopos depositados internamente.

(2) No se han podido descubrir alteraciones hematológicas en la circulación

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The Clinical Sequence of Physiological Effects of Ionizing Radiation in Animals¹

C LADD PROSSER, Ph D

With Contributions by

E. E. PAINTER, Ph D, HERMANN LISCO, M D, AUSTIN M. BRUES, M D, LEON O. JACOBSON, M D,
and M. N. SWIFT, M S

IONIZING radiations constitute a useful therapeutic and experimental tool but, at the same time, a dangerous one. The increase in availability of sources of radiation with modern advancements in the field of nuclear energy makes possible the inadvertent exposure of many more people than was ever possible when x-ray tubes and radium constituted the principal known sources of radiation. In the event of an atomic war, entire populations will be subjected to radiation hazards. Radioactive materials deposited in the bodies of workers in the atomic energy industry may cause many disabilities. It is increasingly important, therefore, that the clinical effects of radiation be understood and methods of therapy be explored and made available.

Researches in clinical physiology and biochemistry at the Metallurgical Laboratory have been concerned with (1) ascertaining whether different kinds of ionizing radiation have similar effects upon the mammalian body, (2) measuring sensitive reactions as a function of dose, in the hope of setting permissible exposure limits, (3) searching for sensitive biological indicators of exposure, (4) describing the course of radiation damage sufficiently to suggest profitable directions for research into mechanisms of such damage that might eventually lead to effective therapy. None of these objectives has been attained in a final form, but sufficient data are available to justify a summary at this time.

Extensive reviews of the pre-war experi-

mental literature on the effects of x-radiation upon animals have been published by Dunlap and Friedman in Shields Warren's monograph (1942-43) on the *Pathology of Radiation*. The emphasis in the present paper is upon work done in the Health Division of the Metallurgical Laboratory. The collaboration of numerous persons has made possible a wide variety of physiological and biochemical measurements on individual animals. Contributions by the following persons should be acknowledged: E. E. Painter, M. N. Swift, and Owen France, physiologists; Austin M. Brues, Samuel Schwartz, and Margaret Rand, biochemists; Leon O. Jacobson, hematologist; Hermann Lisco, pathologist; J. G. Allen and Donald Buchanan, clinicians; G. Sacher, statistician, and numerous technicians who have carried out much of the detail of the experiments.

The general pattern of the clinical effects of radiations in several species falls temporally into the following periods: (1) initial, (2) acute, (3) subacute, and (4) chronic. The manifestations of each period differ somewhat according to species, and the periods should be distinguished by clinical course rather than by specific times.

Direct evidence for temporal differences in clinical effects is provided by the observation that for a given dose rate, but different duration of exposure, e.g., different total doses of single lethal exposure to total body x-irradiation, deaths occur in waves. In the rabbit, for example, peaks

¹ The work reported herein was done in the Metallurgical Laboratory, University of Chicago, under the Manhattan Project. This paper is a brief version of material to be published in the Plutonium Project Record of the Manhattan Project Technical Series. Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

periférica de ratones, conejos y cobayos con una exposición diaria de todo el cuerpo a 0.1 r de radiación gamma durante más de tres años, aunque en los ratones expuestos crónicamente a una dosis de dicha magnitud se presentan tumores ováricos.

(3) Los cobayos revelan una disminución equívoca en las cifras linfocitarias tras la exposición diaria crónica de todo el cuerpo a 1.1 r al día, mientras que los conejos, ratones y cobayos expuestos a dosis de 2.2, 4.4 u 8.8 r muestran significativas alteraciones hematológicas al cabo de períodos variables de tiempo. El cobayo es el animal más sensible, el ratón ocupa un puesto intermedio y el conejo es el más resistente en lo tocante a alteraciones hematológicas provocadas por la irradiación.

(4) Los seres humanos sometidos a una exposición de todo el cuerpo a los rayos X, que representaba 300 r (dosis cutánea), administrados a dosis diarias fraccionadas de

5 a 20 r, revelaron una sensibilidad del aparato hematopoyético más o menos comparable a la del cobayo y el perro.

(5) En los estudios llevados a cabo en el personal del Proyecto del Plutonio, no se observaron alteraciones hematológicas imputables a la exposición a la radiación correspondiente a la "escala de tolerancia."

(6) Se necesitan con urgencia pruebas clínicamente aplicables para determinar y justipreciar las lesiones incipientes debidas a la exposición del personal a la radiación en la "escala de tolerancia." Es peligroso atenerse a estudios de los componentes hematológicos de la sangre periférica, pues no cabe esperar hallazgos con una exposición en esa escala. Debe considerarse como grave la aparición de alteraciones hematológicas imputables a la exposición aguda o crónica a las radiaciones, y probablemente debe vedar toda exposición ulterior del individuo afectado.



a dose of x-radiation in the midlethal range. In rats, the food consumption is reduced but the water intake is increased in this period. In the rabbit, fecal output is diminished but there is usually a polyuria for one to three days. In rats, the initial polyuria is even more extreme than in the rabbit, this is undoubtedly correlated with the concurrent polydipsia in the rat. In dogs, the initial reduction in food and water consumption may be reflected in a smaller reduction in urine and feces output. During the first two days after injection of doses of Sr^{89} or Pu^{239} , which are lethal in two weeks (Sr at $1\mu\text{c}/\text{gm}$ or Pu at $0.075\mu\text{g}/\text{gm}$), dogs show little change in food and water consumption.

Weight loss in the rabbit during the first two days is considerable (more than 8 per cent after 800 r), weight loss begins in the rat at this time, but the dog rarely shows any significant early decrease in weight. If food and water balance is used as a criterion, the initial reaction is more severe in the rabbit, less in the rat, and least in the dog.

Circulatory System The peripheral vascular reaction is shown by the erythema that appears in man during the first day after local skin doses of a few hundred roentgens. In rabbits that receive local doses of 800 to 1,200 r there is some hyperemia, with an increased spread of intradermally injected Evans blue dye, T-1824. There is also accelerated appearance of this dye after intravenous injection.

In rabbits, the blood pressure falls rapidly to a minimum at one and a half to three hours following x-irradiation. The reduction is as much as 50 per cent after 600–800 r, and a detectable fall in blood pressure occurs after 50 r. In some rabbits the blood pressure continues to fall and death results, in others a gradual recovery of blood pressure occurs. Dogs show no alteration in blood pressure or heart rate during this initial period. Blood volume measurements in rabbits, by the use of Evans blue, T-1824, showed no significant changes during the first four or five hours.

Hematology During the first two to twenty-four hours after x-irradiation, a leukocytosis occurs in some species. This leukocytosis has been found by Jacobson to be predominantly a granulocytosis in the rabbit and the chicken. Not sufficient counts have been made during the first day to show whether or not an initial increase in heterophil count occurs in the dog. In the rabbit, after 600–800 r, the peak of the heterophil count comes at twelve to twenty-four hours and is higher than at low doses (300–600 r), where the peak comes earlier. In all species a severe lymphopenia begins within a few hours after exposure. After granulocytosis in the rabbit (probably immediately in the dog), there is a marked decrease in the number of granulocytes per cubic millimeter. In the dog, a reduction of 60 to 80 per cent in lymphocytes and of 40 to 60 per cent in heterophils occurs by the twenty-fourth to forty-eighth hour after a midlethal dose (300–350 r).

After the injection of acutely lethal doses of Sr^{89} or Pu^{239} , the lymphopenia and granulocytopenia may be nearly as great after one or two days as after a lethal dose of x-radiation. No leukocytosis has been observed in rabbits twenty-four hours after injection of lethal doses of Sr^{89} , Ra , or Pu .

Causes of Initial Reactions The physiological factors leading to the preceding reactions are multiple. The skin vessel reactions are local and direct. The lymphopenia is in large part due to direct killing of lymphocytes in nodes and other lymphoid tissue. The gastro-intestinal symptoms are largely direct, since it is generally found that irradiation sickness seldom occurs when the abdomen is shielded. The altered food and water intakes are probably associated with the gastro-intestinal changes. The fall in blood pressure, that may lead to death in rabbits, is in part an autonomic reflex, as shown by partial protection by vagotomy or atropinization, and is, in a measure, due to the indirect action of toxic agents as shown by transfusion experiments. Plasma histamine apparently increases slightly in the rabbit. Antago-

in mortality at the midlethal λ -ray range (800 r) occur at five to forty-eight hours and ten to fifteen days, and scattered deaths are seen at thirty-five to ninety days. In rabbits, mice, rats, and dogs, the majority of acute irradiation deaths from single λ -irradiation or high level daily λ -irradiation (e g, 25 r daily to the dog) or from injected materials such as Pu^{239} or Sr^{89} , occur during the period of ten to twenty-one days after treatment.

When the mortality rate is plotted as a function of dose rate for different daily doses of λ -radiation, discontinuities occur that suggest different mechanisms of killing. It is one purpose of this report to identify some of these mechanisms. In practice, the clinician may have to deal with patients who have been exposed to dose rates ranging from the radiation flash of an atomic bomb detonation to the dose accumulated over a period of years from a small amount of radioactive material deposited in the body.

In general, the clinical course is similar whether ionization is caused by penetrating external radiations or by radiations from internally deposited materials. Since more data are available from λ -irradiation than from other types, most of the following account will refer to λ -irradiation unless otherwise stated. The initial and acute effects are best seen at median lethal (30-day) and slightly lower doses. The 30-day MLD for single doses of λ -radiation in our laboratory is for dogs 325 r, goats 350 r, rabbits 800 r, rats 600 r, mice 530 r.

INITIAL REACTIONS

One of the most striking characteristics of irradiation damage is the latency of the reactions. The primary reactions at the time of the ionization start long chains of events. We are concerned here only with the late links in these chains. At sufficiently high dose rates (greater than 100 r per minute) deaths may occur "under the beam," i e, during exposure. Several examples of killing at very high dose rates have come to the authors' attention and will probably be published subsequently.

Henshaw (1944) gave doses of 25,000 to 50,000 r of λ -radiation at 250 r per minute to mice, rabbits, and guinea pigs. The animals were killed during exposure or died a few hours later. Histologically, there was widespread tissue damage, muscle spasticity appeared to precede rigor mortis. Mice exposed to an intense source of gamma radiation by Henshaw and Curtis died during twenty minutes of exposure. It is possible that such ionization densities may be sufficiently great to cause damage to cell membranes that are relatively unaffected at lower dose rates.

At lower dose rates, (e g, 5 to 15 r/min.), a series of reactions appear during the first twenty-four hours after an exposure to a total dose of 50 to 800 r total body λ r radiation. These initial reactions are sufficiently severe so that some deaths occur in rabbits and chickens in this period when an MLD is given. No deaths have been reported to occur at this time in rats, mice, guinea-pigs, dogs, or goats. These latter species, however, do show initial symptoms that are less severe than those in rabbits and chickens.

The initial reaction after irradiation of the entire body or a large part of the body, in most species, is shock-like prostration, diarrhea, urination, and lacrimation. In addition, vomiting occurs in the dog, and nausea and vomiting in man. In the rabbit, there is extreme prostration with a marked fall in blood pressure and leukocytosis.

Gastro-Intestinal Symptoms The gastrointestinal effects are severe as indicated by the diarrhea, nausea, and concomitant anorexia. The gastro-intestinal tract shows increased tone and motility during exposure to λ -radiation along with and followed by a transitory increase in gastric acidity, as shown by Ivy in 1923. In the rat, Dr Barron and Dr France found that intestinal absorption of glucose introduced into the stomach is completely inhibited four hours after doses as low as 50 r.

Food and Water Balance The intake of food and water is reduced for one to two days after exposure of dogs and rabbits to

minimum at 2-4 days in dogs. A significant lymphopenia can be detected in dogs and rabbits after single λ -irradiation of 25 r. In dogs, a 60 per cent reduction occurs after 50 r, after an injected dose of Sr^{89} at $0.1 \mu\text{c/gm}$, or an injection dose of Pu at less than $0.075 \mu\text{gm}$ ($0.00468 \mu\text{c}$)/gm. This lymphopenia is greatest at all doses at about fifteen to twenty days, although the daily reduction after the first day is small. In survivors, the lymphocytes recover very slowly over a period of three to six months after midlethal doses of λ -ray in dogs and over a two-month period in rabbits.

The initial granulocytosis of the rabbit and chicken is changed to a reduction in granulocytes, this reduction in granulocytic components in all species continues for several days, reaching a minimum count at four days in rabbits, at five days in rats, and at twelve to eighteen days in dogs. A similar time course of the blood picture occurs in the dog after daily λ -irradiation at 50 r and 25 r and in the dog, mouse, and rat after acutely lethal doses of injected materials such as Sr^{89} and Pu^{239} . At sublethal doses, the minimum granulocyte count occurs at about the same time as in non-survivors. Recovery is nearly complete after midlethal doses of λ -radiation in the dog at fifty days, and in the rabbit at twenty-three days. The response of the heterophils has a higher threshold than that of the lymphocytes. 100-200 r in rabbits and approximately 50 r in the dog. After injections of Sr^{89} the heterophils are relatively more diminished than are lymphocytes in all species, due to the relatively greater irradiation of bone marrow.

In general, eosinophils show a response similar to that of the heterophils. Monocytes are decreased rapidly in number and return to normal more slowly than do heterophils in the dog.

Blood platelets also decrease in number and, in dogs, reach minimal levels about a week later than the granulocytes. A significant reduction in platelet count occurs at 50 r in dogs. More than a 50 per cent reduction occurs in rabbits after 500 r.

It is of interest to note that lymphocytes and granulocytes are minimal in number in all animals at the time when most deaths occur, also the relative effectiveness of λ -rays in rabbits and dogs to cause lymphopenia and death is similar. It does not follow that death is due to the leukopenia, but certainly the defense mechanisms are reduced, and frequently a brief infection leads to death.

An anemia is produced more slowly than the leukopenia, in non-survivors (acute deaths) the anemia develops more rapidly during the last week of life. In survivors of single doses of λ -radiation, a minimum red count occurs late—at fourteen days after exposure in rabbits and three and a half weeks in dogs. Below 100 r neither of these species shows a significant anemia. Recovery is more rapid in the rabbit (twenty-three days) than in the dog (two or three months). After acutely toxic doses of such agents as Sr^{89} and Pu^{239} , the minimum red cell count occurs in survivors at a period later than the time of death of non-survivors. The reduction in red count is greater in the survivors than that at the time of death of the non-survivors. This reduction in number of red cells per cubic millimeter is in part due to cessation of production of erythrocytes, as indicated by the virtual absence of reticulocytes after the first day following doses of 200 r or higher in the dog. Upon recovery, survivors of doses in the midlethal range show an elevation in reticulocyte count above the control level. The reduction in red cells is also partly due to their destruction in excess of the normal rate. Calculations based on plasma volume and hematocrit measurements show that, in the dog, three weeks after doses of 200 r or higher, 20 to 40 per cent of the original red cells are destroyed. This excessive destruction of red cells is also indicated by a maintained increase in excretion of fecal urobilinogen and of urinary bilirubin. Similar cessation of production and excessive destruction of red cells were found after treatment with acutely lethal doses of Pu and Sr. In general, the fall and recovery of hemoglobin in

nism by repeated injections of adrenalin protects against lowering the blood pressure, and this antagonism should be useful in therapy. The granulocytosis is probably a response to toxins liberated at the time of treatment or shortly thereafter. According to Bloom and his associates, there is more cellular damage in the first few hours in the rabbit after an MLD (800 r) than in a rat after an MLD (600 r). It is of interest that the granulocytosis and cell death are greatest in the rabbit, an animal that shows the most violent initial reaction as judged by vascular and metabolic changes.

The initial shock reaction, then, is manifested by gastro-intestinal, circulatory, hemopoietic, metabolic, and biochemical alterations. Other organ systems may also be damaged. In lack of specificity, the reactions resemble those due to numerous toxic agents. The above effects were seen after α -irradiation but they could probably be duplicated with comparable doses of other kinds of radiation. Most of the reactions are more severe in those species in which some individuals die in the initial period (rabbits and chickens) than in those that show no initial deaths. Deaths occurred in rabbits in the initial period after abdominal irradiation but not after irradiation of both hind legs, even at doses of 2,400 r. The extent to which these initial reactions start chains that lead to the acute irradiation picture is worthy of investigation.

ACUTE REACTIONS

Early Deaths When the dose rate and the total dose are high, dogs may die in four to six days. Hall and Whipple (1919) observed death four days after massive doses and noted increased excretion of urinary nitrogen, uric acid, and purine base, and extensive gastro-intestinal damage. Moon and his associates (1941) treated dogs with large partial body doses. Within twenty-four to sixty hours these animals showed loss of appetite, vomiting, diarrhea, and traces of blood in urine, feces, and vomitus, they died about twenty-four hours

later. These dogs also showed a terminal hemoconcentration. In our experiments, only one dog (dose 800 r at 12 r/min) has shown such a violent reaction, leading to death in less than one week. Rats at doses of 1,000–1,500 r die in four to five days, whereas at the midlethal dose (600 r) most of them die at nine days. Irradiated rats in general have much diarrhea. It is probable that the early killing at high doses (four to six days in dogs) is accompanied by marked dehydration and that it represents a different course from the initial deaths and the typical acute deaths.

Acute Radiation Deaths The majority of deaths in all species studied after single doses in the midlethal range of gamma or α -radiation delivered at 5 to 15 r per minute, after fast or slow neutron exposure in the cyclotron or in the uranium pile, and after injection with alpha, beta, or gamma emitters, occur nine to twenty-one days after treatment. Acute symptoms are similar for all of these irradiation treatments. Dogs that received daily doses of γ -radiation of 50 or 25 r also died in this period with acute irradiation symptoms. After single lethal doses of γ -radiation following the initial period of shock-like reaction, most species show an intermediate period of days during which relatively few manifestations appear, except leukopenia, until the acute lethal period is approached. In the acute period there are prostration, weight loss, and often a fever such as is seen in a severe toxemia. The physiology of the intermediate and acute lethal periods has been more extensively studied than that of any other period and will be summarized with respect to different functional systems. Most of the following data were obtained after median lethal and lower doses of radiation.

Hematology Leukopenia is probably the most extensively studied irradiation effect both in man and in animals. Hematological studies have been directed in our laboratory by Dr Jacobson. The reduction in lymphocytes which occurred precipitously in the initial reaction continues more slowly after the first day, reaching a

Plasma volume measurements have been made by the use of the Evans blue dye method in dogs that have been treated with λ -radiation, Sr^{89} , and Pu^{239} . As red blood cells are lost from the circulation, the plasma volume increases. This increase may be as much as 15 per cent or more when expressed as per cent of body weight. The net effect is that the total blood volume remains relatively constant. In this rise in plasma volume, the irradiation reaction differs strikingly from traumatic shock.

Gastro-Intestinal Function The delayed absorption of glucose from the gut of rats, which appeared in the initial period, continues. Part of this delay, according to Dr. Barron, may be due to diminished respiration and phosphorylation of fructose by the epithelial cells. Part may be due to delayed gastric emptying, as indicated by retention of traces of non-absorbed yttrium⁹¹ in the stomach two days after x-irradiation. Excessive mucous secretion may also play a part in the delay. The secretion of gastric acid, which was increased initially, has been reported by previous investigators to be diminished by seven days and may be abolished at ten to fourteen days (Ivy *et al.*). Food consumption is only slightly reduced during the intermediate period, but is sharply curtailed in the acute terminal period in all species. Even the rabbit shows recovery from the extreme initial anorexia.

At autopsy, irradiated dogs show extensive hemorrhages in the intestines, both petechial and gross. Ulcers are not infrequent. Infections in the mouth and pharynx are often seen. These pathological findings are less frequently seen among rodents, although in these animals the gut may be hyperemic. Intestinal hemorrhages and ulcers have been found in dogs that died acutely from Sr^{89} and Pu^{239} . These latter effects are surprising, since these elements localize largely in bone and the direct irradiation of the gut must be small. A terminal diarrhea has been noted in all species.

Kidney Function In dogs, urinary excretion of water and nitrogen is maintained

at fairly normal levels even when intake is reduced after irradiation. Terminally, water and nitrogen loss exceeded intake. Urinary specific gravity remained relatively constant. Phenol red clearance was measured at intervals before and after irradiation in 5 dogs that received midlethal doses of λ -radiation, and creatinine clearance was measured in one dog. In each of these, there was increased clearance during the few days prior to the terminal period, *i.e.*, nine to thirteen days after irradiation. These experiments should be extended and clearance of other materials measured. At the same time the blood non-protein nitrogen declined by 25 to 50 per cent, the urea nitrogen by 20 to 30 per cent, and "polypeptide nitrogen" by about 25 per cent. This non-protein nitrogen decrease is more probably due to increased output than to any decrease in protein breakdown. These three lines of evidence—(1) maintained water and nitrogen excretion, (2) increased phenol red clearance, and (3) decreased blood non-protein nitrogen—suggest increased kidney function in the intermediate period. This may be a reflection of increased blood flow.

Terminally, however, a marked increase in blood non-protein nitrogen, urea nitrogen, and polypeptide nitrogen suggests a late diminished kidney function which may be, in part, a result of failing circulation. In a small series of dogs, only those that showed the terminal rise in non-protein nitrogen died. Hemorrhages were frequently seen in the kidney at autopsy.

Water Balance During the first seven to twelve days after a single midlethal dose of x-radiation or of Sr^{89} or Pu^{239} , certain small alterations in food and water exchange appear that become greatly accelerated in the terminal period. It was stated above that, during the first day, water intake is markedly reduced in rabbits, may be slightly reduced in dogs, and is decreased in rats, while urine output is little changed in dogs and is temporarily increased in rabbits and rats. The reduction in water intake, in the face of maintained or increased urine output, would lead to de-

grams per cent and volume of erythrocytes in per cent of blood volume parallel the changes in the red cell count. In none of these animals (dogs and rabbits) are there changes in mean corpuscular volume or in mean corpuscular hemoglobin during the acute period. The maximum acute reduction in red cells is less than 50 per cent. The minimum occurs later than the peak of deaths, hence anemia can hardly be a causative factor in acute irradiation deaths.

At about one week after a midlethal dose of γ -radiation, the sedimentation rate increases markedly. This increase, which may be as much as 70 times, is seen also after internal irradiation by Sr^{89} beta rays or Pu^{239} alpha rays. Dogs usually die with a high sedimentation rate, whereas in survivors, sedimentation returns to normal in about one month after a maximum speed of sedimentation at fifteen to twenty days. The threshold in dogs for increased sedimentation rate is 100 r. The increase in sedimentation is partly due to decreased volume of erythrocytes (hematocrit) but, in addition, is due to some factor in the plasma that accelerates the process.

Approximately one week after a midlethal dose of γ -radiation, Sr^{89} , or Pu^{239} , dogs show delayed clotting of the blood. Clotting time may lengthen by two to four times after doses of 200 r or above. Dr. Allen has found that this is not directly correlated with the platelet count, but is due to an increase in free heparin in the blood, for addition of toluidine blue, which complexes with heparin, shortens the clotting time. Prothrombin time is not altered. Vitamin K and transfusions of whole blood were ineffective in reducing clotting time.

Cardiovascular Function. In rabbits after recovery from the initial reduction, the blood pressure remains relatively constant but is lower than before irradiation. In dogs, there is no change in blood pressure in the initial or intermediate periods. Several days before death, however, both animals enter an acute terminal period in which the blood pressure is reduced.

At this time the heart rate of dogs increases by as much as 50 per cent, and the

rectal temperature rises by about 2°C . In dogs that survive, there may be a transient elevation of heart rate and rectal temperature in the third week, the threshold for this reaction in dogs is about 250 r. In some rabbits, there is a rise in temperature in this acute terminal period, in others, there is no change. In most rabbits there is a final fall in temperature as the circulation becomes sluggish. A similar terminal period of elevated heart rate and temperature and depressed blood pressure has been seen in dogs injected with acutely lethal doses of Sr^{89} and Pu^{239} .

Capillary dilatation is a consistent finding in acute irradiation injury. In the skin, this results in a second wave of erythema at ten to twenty days. It may be accompanied by swelling of vessel endothelial cells, stasis, extravasation of blood, and even by rupture of vessel walls.

In the preterminal period, subcutaneous hemorrhages can be seen in most species, there is often rectal and oral bleeding. Hematomata form readily. Part of this bleeding tendency is probably related to the delayed clotting reaction and decrease in platelets. These factors alone, however, are insufficient, in that there is often no good correlation between them and bleeding, it becomes necessary to postulate an increase in capillary fragility. The acute bleeding tendency was noted extensively among persons irradiated at Hiroshima and Nagasaki (Warren, 1946). Dogs and goats injected with Sr^{89} showed hemorrhages in the parietal pleura over the ribs, they also showed some hemorrhages elsewhere, but these local ones in the vicinity of the ribs indicated a direct effect of irradiation upon capillaries.

At autopsy, evidences of hemorrhage are frequently found in the gastro-intestinal tract, lymph nodes, scattered subcutaneous areas, and often in the heart. The hemorrhages of the heart may vary considerably in location and size.

Prior to death, the heart may be injured, as shown by a lowering of the take-off level of the T-wave. This may result in a reversal of the T-wave.

Measurements of metabolic balance after injections of radioactive materials are less extensive than after x-irradiation, but the general picture appears to be similar. The effect of irradiation appears to be an acceleration of normal catabolism, particularly in the acute lethal period. The correlation between the terminal negative nitrogen balance and death is very striking. If it were possible to prevent tissue destruction that occurs about two weeks following irradiation, it might be possible to prolong life.

Plasma Proteins Total plasma protein is diminished by a few tenths of a per cent during the intermediate period. In the terminal acute depression period, there is a rise in protein which, like the rise in non-protein nitrogen, is not found in survivors in the median lethal range. Since plasma volume increases, there is an increase in total circulating protein, hence the increased concentration is not attributable to dehydration. The high plasma protein terminally may be associated with tissue breakdown. Electrophoretic analyses by Dr. Muntz show that at the time when fever first appears, serum albumin becomes reduced by about 50 per cent, whereas α_3 and α_4 globulins and the β globulin-fibrinogen fractions double in amount. These changes in the protein pattern have been seen in dogs treated with acutely lethal doses of x-rays, Sr^{90} , and Pu^{239} . They also appear in other conditions, such as distemper. Injections of albumin at the time when plasma albumin was low failed to cause reduction in the globulins.

Blood Sugar, Cholesterol and Phosphatase There are more reports in the literature of an increase than of a decrease in blood sugar immediately after irradiation. Blood sugar was increased for several days prior to the onset of fever in dogs. During the fever normal values were found. The explanation of the high values in the intermediate period is not evident.

Cholesterol in the blood remained constant until the terminal period was reached, when it increased significantly in dogs that were receiving daily x-irradiation, as well

as in dogs injected with Pu. We made no measurements after single irradiation.

Acid and alkaline phosphatase were determined in the blood of several dogs given daily irradiation, neither showed much change until the acute terminal period, when the alkaline phosphatase increased.

Liver Function Liver function and hemoglobin metabolism have been studied by Dr. Schwartz and his associates. Increased red cell hemolysis is indicated by elevated excretion of fecal urobilinogen and urinary bilirubin. When food intake is diminished, the urine and plasma often become yellowish green, due presumably to diminished reduction of biliverdin to bilirubin by the glycogen-poor liver. This becomes especially marked during the several days before death. Liver dysfunction in irradiated mongrel dogs is also shown by a marked increase in the ratio of uric acid to allantoin in the urine. Spectrophotometric analysis of urine showed an increase in excretion of kynurenic acid as dogs entered their terminal period, this suggests altered tryptophane metabolism.

A marked decrease has been found in the excretion of urinary and fecal coproporphyrin during the early and intermediate periods. Though the exact mechanism of this decrease is not clear, it is possible that it may be due to diminished erythropoiesis. A terminal increase in excretion of coproporphyrin is believed due to liver damage.

Respiratory and Nervous System The nervous system is well known to be resistant to irradiation. Grossly, no dysfunctions of the respiratory or the nervous system have been seen during the intermediate period. Terminally, breathing becomes labored and diaphragmatic, the oxygen content of drawn blood is below normal. Some six to twelve hours before death, dogs frequently show an extensor rigidity, appearing first in the hind legs and progressing to the fore legs. Reflexes are present but may become sluggish. These reactions resemble those seen in hypoxia of the brain. They are undoubtedly secondary.

Nature of Acute Radiation Deaths The majority of animal deaths resulting from

hydration if loss of water from the respiratory tract remained constant

Actually, however, in the dog, the difference between water intake and water loss in urine and feces, *i e*, primarily respiratory water loss, is reduced. In rats the plasma water was slightly elevated ten days after 700 r, and in mice the total body water was increased for at least eight days after 700 r. France found that water deprivation for twenty-four to forty-eight hours before exposure favored survival of irradiated rats. Two to four days before death, water intake is much reduced in all species, and the ratio of intake to output is less than previously. Thiocyanate space in rats increased by about 2 ml/100 gm during two weeks after 400 and 700 r, and for a few days after 200 and 100 r. A similar increase in SCN space was found in two dogs after 400 r, but not in two after 250 r. Hemoconcentration has never been observed in this laboratory in the intermediate and acute period. The volume of erythrocytes (hematocrit) and plasma protein decline during the intermediate period.

When animals approach the acute period, edema is frequently observed, especially in the face, neck, and extremities. The intestinal wall is often found edematous at autopsy.

All of these observations indicate that, after acute lethal irradiation, water intake of mammals is reduced more than is the water loss by urine and feces, however, respiratory loss also appears to be reduced, so that there may actually be some water retention. Extracellular water increases. There is some evidence that dehydration may increase survival. Thus, dehydration may occur in the first few days, particularly at high doses, but hydration appears in the intermediate and acute period and at midlethal and lower doses.

Metabolic Balance Direct measurements of basal metabolism have not been made in animals after irradiation. An indirect approach has been made, however, by subtracting the net water balance from the total insensible loss (food and water balance) in dogs. This difference approx-

imates the combination of carbon dioxide expired and body water lost. An increase was noted during the first two weeks after x-irradiation (at midlethal doses) and a greater increase during the terminal period, apparently there is a net increase in metabolic breakdown.

Weight loss was greatest in the first few days after irradiation in rabbits. In dogs, there was little weight change seven to ten days after a midlethal dose, but thereafter some 20 per cent to 50 per cent of the initial weight was lost. In rats, the weight loss was more gradual during the intermediate period and was abrupt during the last few days of life. When the weight loss in irradiated dogs is compared with that in non-irradiated dogs in which the food intake has been reduced to match or be less than that in irradiated dogs, greater weight loss is found in the irradiated animals. This observation indicates an increase in tissue breakdown, due to irradiation. Calculation of the protein component of the weight loss based on nitrogen balance measurements indicates that the protein component is similar in irradiated dogs and in dogs on a restricted intake, being about 10 per cent of the total weight loss in each.

A third type of evidence of increased tissue breakdown comes from measurement of blood nitrogen and of nitrogen balance. In the intermediate period there is usually a slight decline in non-protein nitrogen in the plasma. Terminally, however, the blood non-protein nitrogen increases steeply. Plasma urea nitrogen goes through the same intermediate decrease and terminal rise, but by smaller amounts. Nitrogen excretion is maintained or even increased after intake is diminished in the late period of anorexia (several weeks). However, on the last day or two little urine is formed, this can account for a small portion of the rise in blood non-protein nitrogen at that time. During the acute terminal period (fever, etc.), nitrogen balance is negative. At this time, there is a toxemia which may be due in part to some unidentified components of tissue breakdown.

The results presented above add strength to the general conclusion that the acute terminal state is one of a non-specific toxemia. In the intermediate period, altered function has been shown for many organ systems. These again are non-specific effects, and no single change (except for leukopenia) is great enough to result in the terminal toxemia that appears so abruptly. The relation of each of the changes in the initial and intermediate periods to the reactions of the acute terminal period should be established experimentally.

THE SUBACUTE RADIATION REACTION

Some animals show signs of the initial and acute reactions but survive beyond the acute period and continue to live on into a subacute phase. Subacute deaths have been seen in dogs that died after about three months of λ -irradiation at 12.5 r daily, and in dogs that died ninety days and two hundred and thirty-four days after an injection of plutonium. No dogs have died subacutely after single doses of λ -radiation, although some rabbits die subacutely during the period of thirty to one hundred and fifty days after such doses. A subacute death has occurred in one goat forty-eight days after an injection of Sr^{89} .

In the dogs that died after daily λ -irradiation of 12.5 r and in one at 25 r daily, the reduction in white cells was less severe terminally than in the acute (higher dose rate) deaths but the anemia was much more severe. Other signs such as diminished appetite, weight loss, elevated sedimentation rate, and prolonged clotting time did not appear until most of the lethal dose had been accumulated. The terminal sequence resembles that in acute irradiation death (fever, increased heart rate, etc.). Chemical determinations on blood showed no significant changes (except for a gradual rise in blood cholesterol) until the terminal period. Hemorrhages were fewer than in acute deaths. The hemoglobin reached less than 4 gm per cent in each of these dogs. The bone marrow was strikingly aplastic. The dog that died ninety days after an injection of Pu re-

sembled those that died after a similar period of daily λ -irradiation, except that the anemia was slightly less severe. The goat that died forty-eight days after injection of Sr^{89} had a terminal hemoglobin of 1.5 gm per cent and a red cell count of 2,920,000 cells per cubic millimeter, compared with pre-injection values of 9.0 gm per cent and 9,980,000 red cells. The mean corpuscular hemoglobin remained relatively constant in all of the dogs that died subacutely, but the mean corpuscular volume increased in the dogs receiving 12.5 r daily and in those that ultimately died subacutely from Pu. The earliest human deaths from radium poisoning, as reported by Martland (1931), were due to anemia—hyperplastic marrow with immature cells in the circulation. One type of subacute irradiation death, therefore, is due to anemia. The white count is low but often not so low as in the acute deaths.

Rabbits that die several months after a single dose of λ -radiation usually become severely emaciated. Only scattered blood counts are available, but these fail to show any significant anemia or leukopenia. Rabbits that die at ten to fifteen days usually lose 15 to 20 per cent of their initial weight before death. A group of rabbits that died forty-five to sixty days after 800 r λ -irradiation lost an average of 37 per cent (range 21 to 46 per cent) of their initial body weight. Quantitative data are not available on a large number of rabbits, but the records of rabbits dying subacutely after λ -irradiation indicate occasional infections and general extreme emaciation. One dog died two hundred and thirty-four days after an injection of Pu, this dog lost 37.8 per cent of its initial weight. Terminally there was an accumulation of ascitic fluid and the liver was atrophic. This animal showed no late anemia or leukopenia. The bone marrow was hyperplastic but no immature forms were seen in the peripheral blood.

A third type of subacute effect has been described by Lisco and Brues in rats and mice injected with plutonium and radium. Some mice at doses of Pu at

massive doses of external or internal irradiation occur at two to three weeks. Apparently most of the irradiation deaths at Hiroshima and Nagasaki and two deaths at Los Alamos occurred in this same time. The terminal picture in all of these deaths suggests a toxemia. There are fever with elevated heart rate (dogs and man), prostration, evidence of circulatory failure, and anoxia. Three possible sources of toxins are (1) extravasated blood, (2) products of tissue breakdown, (3) infectious agents.

Extravasated blood is present wherever local hemorrhages occur, edema is often noted, and is frequently bloody. The bleeding tendency is favored by delayed clotting, increase in free heparin, low platelet count, and probably capillary fragility. Therapy should be directed toward preventing bleeding. The amount of blood lost in this way, however, is not great, and in rodents the hemorrhages are often difficult to find, hence, it is questionable whether extravasated blood is an important toxic factor.

Tissue breakdown is certainly significant. Weight loss is in excess of that due to restricted intake, the net metabolic loss increases, nitrogen excretion is constant or increases in the face of diminished intake. For a time (before the fever) the kidneys seem to increase their total output as indicated by increased phenol red clearance and possibly reflected in falling non-protein nitrogen, but in the last day or two of life, non-protein nitrogen accumulates and blood protein concentration increases. Whether there are any specific toxins or whether terminal kidney failure allows normal waste products to accumulate to toxic concentrations is not known. Survivors fail to show either the late rise in non-protein nitrogen and protein or as great a weight loss as non-survivors. This indicates the importance of tissue breakdown and kidney failure terminally. Research should be initiated toward understanding the nature of the accelerated catabolism and toward attempts to restrain it. *In vitro* studies of tissue metabolism by Bar-

ron and his associates indicate inhibition of some enzymes, particularly SH-containing ones, but do not indicate increased enzymatic catabolism. We found that survival of mice was favored by prior treatment with nicotinamide, DPN, and ascorbic acid, but not by thiamine, pyridoxine, or riboflavin, the nicotinamide, when given after irradiation, did not aid animals.

Infectious agents cannot be disregarded as sources of toxins. At Hiroshima and Nagasaki secondary infections, particularly of the respiratory tract and lower bowel, were common according to Shields Warren's published account. There are frequent ulcers in the mouth and intestine, infections of tonsils and nasal passages, and sometimes open skin lesions in irradiated dogs and goats. The leukopenia favors the multiplication of organisms already present in the body. The degree of leukopenia in the middlethal range is consistently greater terminally than in survivors at the same time. Indications of bacterial invasion have been found by several earlier workers. It is not always possible, however, to find foci of infection in dogs and goats, and in rodents, the foci are less frequent. Only a few rabbits have shown terminal fever. Infections are generally less important in rodents than in dogs, goats, and man. Therapy in man is indicated in the direction of increasing the body defenses in number of white blood cells and immune bodies. In a few attempts to inject suspensions of white blood cells, these cells were rapidly removed from the open circulation. Replacement by transfusion is difficult and requires very large amounts of blood. Intraperitoneal injections of isotonic saline, and to lesser extent ascorbic acid and pentnucleotide, after doses of 600 r in rabbits have hastened the recovery of white blood cells, liver extract and a bone marrow preparation were ineffective. These agents failed to increase the survival of mice when they were injected after irradiation, although ascorbic acid was slightly beneficial when given repeatedly for several days before irradiation.

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0 00312–0 0312 $\mu\text{c/gm}$ and some rats at doses of Pu at 0 0025–0 065 $\mu\text{c/gm}$ die of a liver disease eighty to three hundred days after injection. Terminally they show typical symptoms of hepatic insufficiency such as jaundice and ascites together with characteristic pathological lesions of the liver. Similar effects are seen in rats injected with radiocerium at 2 $\mu\text{c/gm}$.

Another effect commonly seen some weeks after the acute period and before chronic effects appear is graying of hair in dark-haired animals.

Dr Norris has found that several months after injection with radium at subacute levels (0 1–1 0 $\mu\text{c/gm}$), mice and rats have calcified arteries. Some rats also have calcified masses in various visceral tissues. These pathological changes indicate a slowly developing disturbance in calcium metabolism after radium injection, they have not been noted following treatment with other radioactive materials. Martland (1931) found that human beings poisoned with doses of radium too low to cause severe leukopenia or anemia often showed pathological lesions in some of the bones. These lesions resulted in extreme fragility of the bone and might lead to death. Similar lesions were seen by Norris in rats four months after injection with radium at 0 5 $\mu\text{c/gm}$.

In summary, subacute deaths occur at lower dose rates and at longer time intervals after massive irradiation than acute death. Aplastic (sometimes macrocytic) anemias and extreme emaciation have been identified as factors leading to two types of subacute irradiation death.

CHRONIC RADIATION REACTIONS

Some animals survive for many months after a single dose of radiation or for many months of continued irradiation—external or internal. They may then die from chronic causes in which leukopenia and anemia may play very little part. Tumors are the most important of these causes.

Tumors do not often result from a single dose of radiation. Lorenz, at the National Cancer Institute, has found an in-

creased incidence of ovarian tumors in LAF₁ mice after a single dose of 50 r of gamma radiation, but he considers these to be secondary to the sterilization of the mice. Raper, Snider, and Henshaw, at Oak Ridge, observed carcinomas in the skin of rats five months after an epulating dose of external beta radiation (5,000 rep). Evidence for an increase in lymphoma after single doses of fast and slow neutrons and after single doses of gamma radiation has been given by Henshaw. In CF₁ mice the incidence of lymphoma ten to twelve months after treatment with 500 r gamma radiation increased from less than 15 per cent in the controls to more than 65 per cent in the experimental animals.

With prolonged dosage at low dose rate, tumors are readily induced. Leukemic mice (C58 strain) exposed to fast neutrons daily for many months showed leukemia earlier than the controls (Henshaw). Daily exposure to gamma radiation at daily doses as low as 11 and possibly 0 11 r/day increased the incidence of ovarian tumors, lymphomas, and lung tumors in LAF₁ mice (Lorenz). External beta rays at 50 rep daily resulted in many skin tumors (Snider and Raper). Mice injected with Pu at doses of 0 05 to 0 1 $\mu\text{c/gm}$ (0 0031 to 0 0062 $\mu\text{c/gm}$), and rats at 0 02 μc and higher, developed many osteogenic sarcomas three hundred to four hundred days after injection. The beta radiation from bone-deposited Sr⁸⁹ also led to an abundance of bone tumors in mice, single doses of 5 $\mu\text{c/gm}$ resulting in tumors after two hundred days and 0 5 $\mu\text{c/gm}$ in four hundred days. When Sr injections were given monthly to bring the dose at the time of each injection up to 1 $\mu\text{c/gm}$, osteogenic sarcomas were abundant after two hundred and fifty days, and at 0 1 $\mu\text{c/gm}$ after four hundred days, a few are appearing after five hundred days of repeated injection at 0 05 $\mu\text{c/gm}$. Similar osteogenic sarcomas were described in persons poisoned with radium for eight to ten years (Martland, 1931). These examples show that, at low dose rates, prolonged irradiation can result in death from cancer.

Other chronic conditions leading to death have not been examined carefully. Henshaw has suggested that irradiation accelerates the "aging" processes in general. Mice and rats that die nine to eighteen months after injection with Sr^{89} or Pu, but without tumors, are often thin, have dull coats, and posturally resemble aged mice and rats. Snider and Henshaw observed that many rats that had received 86 r of gamma radiation daily for nine months were thin and showed some atrophy of lymphoid tissues. A series of dogs have been studied for more than a year after injection with Sr^{89} and Pu at doses such that a mild leukopenia has been maintained. A variety of chemical tests have been totally negative and no tumors have appeared. Better physiological criteria of aging may indicate something of the nature of non-tumorous chronic deaths from irradiation.

GENERAL CONCLUSIONS

Four generalizations can be presented on the basis of the preceding evidence.

I Every kind of ionizing radiation is similar in its clinical action, whether it be penetrating external radiation or internal radiation from deposited material. By appropriate selection of doses, dose rate, and experimental animals, it has been possible to observe a similar clinical course with single and daily x-irradiation, and with internal radiation from deposited alpha and beta emitters. Although it has not been studied in as great detail, the clinical pattern also appears to be similar after treatment with gamma rays, fast neutrons, and slow neutrons. External beta rays may cause skin effects similar to those produced by penetrating rays, but they probably kill by different mechanisms.

II Nearly every organ system is affected by lethal doses of every type of radiation. It has long been known that the most sensitive systems are the blood-forming organs, the gastro-intestinal tract, and the gonads. Peripheral circulation and heart are also affected. Terminally there may be damage to the kidneys and even to

the central nervous system. Some of these effects are probably direct, and some indirect, as a result of toxic agents, or of hypoxia, infections, and other secondary factors.

III No single clinical reaction is peculiarly specific for irradiation damage. A similar preterminal course, with leukopenia and high sensitivity of dividing cells, is found with such toxic agents as the nitrogen mustards, the acute terminal course with fever is similar in acute infections and many diseases. There are striking similarities to anaphylactic shock, and many of the delayed effects of irradiation can be duplicated by various toxic chemicals, e.g., anemia in benzol and phenylhydrazine poisoning and tumor induction by coal tar derivatives.

IV The clinical picture and the conditions resulting in death vary with the dose rate and the duration of exposure for both external and internal radiation. If an animal survives one depression with a given set of symptoms, it is likely to die later from a different mechanism.

A series of clinical patterns leading to death after irradiation have been identified as follows:

(1) Immediate death at very high doses and high dose rates, with general cellular destruction.

(2) Initial shock-like death seen within forty-eight hours after x-irradiation in some rabbits and chickens. Initial irradiation sickness is detectable but less severe in other species. General symptoms of the initial reaction are prostration, vomiting, diarrhea, and anorexia. In rabbits there is also marked fall in blood pressure, and in rabbits and chickens granulocytosis and lymphopenia develop. There are vasodilatation, erythema, and generally gastro-intestinal dysfunction.

(3) Early deaths at high doses in dogs and rats (four to six days). There is evidence for dehydration, hemoconcentration, and much gastro-intestinal damage, there is also a leukopenia.

(4) Acute deaths caused by irradiation, which comprise most of the deaths from all

types of ionizing radiations (except external beta rays), occur nine to twenty-one days after treatment. Leukopenia is severe, there is evidence of extensive tissue breakdown, a tendency to bleeding, high sedimentation rate, slight anemia, and altered water balance. The terminal condition is one of toxemia with fever, elevated heart rate, lowered albumin and elevated α_3 and α_4 globulins and β globulin-fibrinogen (dog), high serum non-protein nitrogen, increased serum protein, cardiovascular failure, etc.

(5) Subacute pathological changes leading to death. Five types have been seen.

(a) Aplastic anemia in dogs dying from 12.5 r daily, in a goat at an intermediate dose of Sr^{90} , and in one dog treated with Pu.

(b) Hyperplastic macrocytic anemia seen in patients poisoned with radium (Martland).

(c) Liver degeneration caused by Pu and radioactive cerium in rats and mice (Brues and Lisco).

(d) Emaciation, particularly in rabbits after single doses of γ -radiation and in one dog after Pu.

(e) Bone and bone-marrow lesions as described in radium poisoning (Martland, Norris).

(6) Chronic irradiation deaths. (a) Tumors constitute an important cause of chronic death. Ovarian tumors have re-

sulted from gamma and γ -irradiation, leukemias have been accelerated in appearance by penetrating irradiation, skin carcinomas have resulted from external beta radiation, bone sarcomas appeared after prolonged irradiation with Sr^{90} , Pu, and Ra. (b) Premature "aging," emaciation, and probably numerous other types of chronic irradiation injury lead to death after prolonged exposure at low dose rates.

University of Illinois
Urbana Ill

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SUMARIO

Sucesion Clínica de los Efectos Fisiológicos de la Radiación Ionizante en los Animales

De los experimentos descritos en este trabajo dedúcese que:

(1) Muestran una acción clínica semejante las radiaciones ionizantes de todo género, ya se trate de radiación externa penetrante o de radiación interna procedente de sustancias depositadas.

(2) Casi todos los aparatos o sistemas orgánicos son afectados directa o indirectamente por dosis letales de radiaciones de todo género, pero los más sensibles son los órganos hematopoyéticos, el tubo gastro-

intestinal y los gonados. También se afectan la circulación periférica y el corazón, y al final pueden lesionarse los riñones y hasta el sistema nervioso central.

(3) No existe ninguna reacción clínica única que sea propiamente específica para las lesiones debidas a la irradiación.

(4) El cuadro clínico y las condiciones que culminan en la muerte varían de acuerdo con la dosis y la duración de la exposición tanto con la radiación externa como con la interna. Varios cuadros

clínicos que terminan en la muerte postirradiatoria han sido identificados muerte inmediata tras dosis muy altas y muy segundas, acompañada de citólisis general, muerte parecida al estado de choque inicial en término de cuarenta y ocho horas en algunos animales, muerte temprana (en cuatro a seis días) en perros y ratas, con signos de deshidratación, hemoconcentración, extensas lesiones gastrointestinales y leucopenia, muerte aguda, que comprende la mayor parte de las muertes debidas a toda clase de radiación yonizante (excepto los rayos beta externos), de nueve

a veintidós días después del tratamiento, con grave leucopenia, signos de extensa histólisis, propensión hemorrágica, eritrosedimentación elevada, leve anemia y desequilibrio hídrico, muerte debida a alteraciones patológicas subagudas en forma de anemia aplásica, anemia macrocitaria hiperplásica, degeneración hepática, emaciación y lesiones de los huesos y la médula ósea, muertes asociadas a la irradiación crónica tras prolongada exposición a dosis bajas, presencia de tumores, "envejecimiento" prematuro, emaciación y otras lesiones crónicas debidas a la irradiación



Effects of Total Surface Beta Irradiation¹

JOHN R RAPER, Ph D

University of Chicago

PRIOR TO THE development of the uranium chain reaction and the possibility of obtaining large quantities of artificially produced radioactive isotopes as a direct or indirect result of this reaction, direct experimentation on the biological effects of beta rays were of necessity limited by the availability of pure beta-emitting substances. It has long been assumed, however, that beta rays would produce in biological systems effects identical with those produced by x-rays and gamma rays, since the latter radiations expend their energy by the ejection of high-speed electrons from the atoms of the biological material in which they are absorbed. The validity of this assumption has recently been indicated by the writer and others at Clinton Laboratories in two biological materials which were small compared to the range of beta particles—fern spores and eggs of the fruit fly, *Drosophila melanogaster*. With larger biological objects, however, the distribution of energy absorption differs markedly between beta rays and the more penetrating electromagnetic radiations, and consequent differences in effect are to be expected. In the irradiation of laboratory animals with beta rays from external thick phosphorus³² sources, all of the energy is absorbed in a superficial layer of tissue which in the mouse comprises about one-third of the animal's volume, in the rat about a sixth, and in the rabbit only about one-twentieth. Thus, in effect, total surface irradiation with beta rays furnishes a means of studying the effects of high doses of an ionizing radiation delivered almost exclusively in larger animals to a single organ, the skin (Fig 1).

"Envelope" or "cosine" thick phos-

phorus³² sources were used for the irradiation of laboratory animals. The exposure chambers consisted of plastic boxes lined with panels of phosphorus-Bakelite which were activated in the Clinton Pile by the reaction $P^{31}(n\gamma)P^{32}$. An animal confined within such an emitting enclosure received an equal dosage of beta rays over its entire surface.

In order to explore fully the effect of energy absorption distribution on biological effect, laboratory animals, including mice, rats, guinea-pigs, rabbits, and one-day-old baby rats, were exposed at graded doses in sufficient numbers to establish the pattern of effects in each species. It will be possible here to give only a brief synopsis of the major lines of endeavor and to point out some of the more significant results which were obtained in this work.

Due to the superficial absorption, irradiation with beta rays in doses below the acute lethal range results in greater gross and superficial damage than that following irradiation with the more penetrating x-rays or gamma rays. The pattern of gross damage can best be shown by the incidence of the various effects, with time following irradiation, in a group of animals which received identical doses (Fig 2). A single dose of 4,000 rep (roentgens equivalent physical) delivered in about an hour, first produces visible damage in mice about a week after irradiation, at which time the eyelids become inflamed, the eyes watery and, in a large percentage of individuals, sealed shut. A few days later, epilation around the eyes and snout becomes evident, and by the end of three weeks all animals are similarly and conspicuously affected. A slight erythema on the feet and ears

¹ The work reported herein was done by the author, Cpl K K Barnes, Dr R E Zirkle, Dr J E Wirth and Dr H J Curtis, at Clinton Laboratories, Oak Ridge, Tenn., under the Manhattan Project. This paper is a brief version of material to be published in the Plutonium Project Record of the Manhattan Project Technical Series. Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec 1-6, 1946.

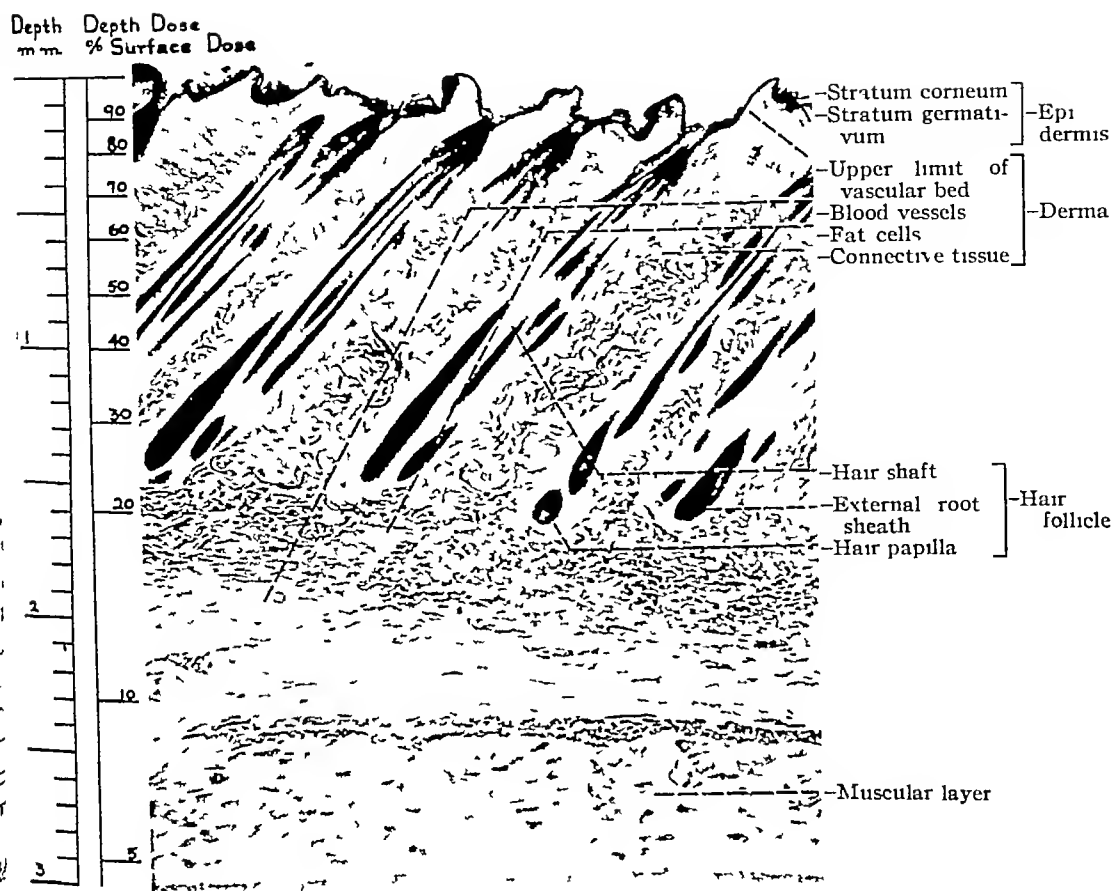


Fig 1 Depth dose of beta rays of phosphorus³² in the skin of the rabbit.

develops in about a third of the animals during the second and third weeks, after which it disappears. Hyperemia and subsequent drying of the ear tips first appear during the third week and are later observed in most of the animals, recovery is complete in most cases but in a few individuals there is complete loss of the tips of the ears. Extensive, and frequently severe, epilation over the entire trunk of the animal begins during the fourth week after irradiation and persists for many months. Concurrent with epilation there may be local desquamation, and the ulcerated areas thus produced frequently persist until the death of the animal.

These progressive changes can perhaps be followed more easily in the pictorial history of a mouse which received 5,000 rep of beta rays on Oct 31, 1944 (Fig 3). The

first photograph in this history was taken two weeks after irradiation and the eyes have opened following earlier closure. Partial recovery from epilation on the trunk and head is evident at six weeks, but subsequent photographs show that such recovery is not permanent. Ulceration, first evident at six weeks on the flank, became more extensive and more severe during the remaining lifetime of the animal. Healing and subsequent breakdown of the skin to form large ulcerated areas are shown strikingly in this history. In the eyes of all survivors of groups of mice irradiated with more than 3,000 rep of beta rays a pronounced opacity developed five to six months after exposure, and from this effect there was no recovery.

Lower doses of beta rays produce in mice essentially the same effects as those dis-

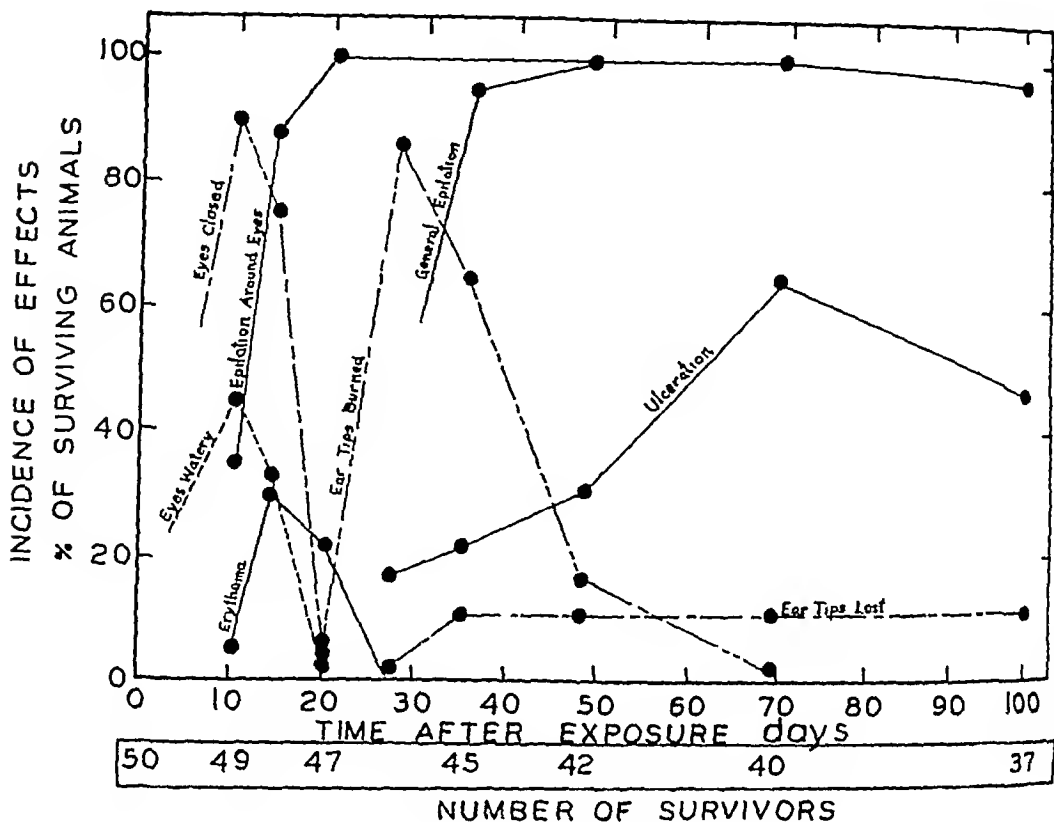


Fig. 2 Graphic summary of damage in mice following a single dose of 4,000 rep of beta rays

cussed for the range 4,000–5,000 rep, but in lower incidence and of less severity. The early effects of higher doses are identical with those in the 4,000–5,000 rep range but paradoxically develop somewhat more slowly than at lower doses, and death occurs before many of the symptoms are manifest. After doses of 10,000–15,000 rep few of the animals show any superficial effect other than watery or closed eyes at the time of death, ten to twenty days after irradiation.

In rats the effects of beta irradiation are similar to those described for mice. Two important differences have been noted, however: (1) to produce comparable damage in the two species, a higher dose, almost double, is required for the rat; (2) the region of most severe epilation and ulceration is characteristically different. In the rat, the head, a medial dorsal band along the spine, and the base of the tail are particularly sensitive (Fig. 4).

Guinea-pigs are less seriously affected

than any of the other species studied. At doses in the acute lethal range the surviving animals showed extensive and severe epilation, but there was no ulceration or loss of ear tips.

The pattern of superficial damage in rabbits at different doses is shown in Figure 5. From these photographs it is clear that the effects are similar to those produced in other species by beta rays, but that the localization pattern of most severe damage differs from those of both mice and rats. At very high doses, 20,000 rep and greater, only closure of the eyes and severe inflammation of the snout region occur before the death of the animal.

Total surface beta irradiation exerts an acute lethal action in each species at a characteristic dosage. The main wave of mortality occurs at a somewhat later post-irradiation time than following irradiation with α -rays or gamma rays, and for lethal studies with beta rays forty-five days has



Fig 3 Gross effects of total surface irradiation with beta rays on mice, exposed to 4 000 rep on Oct. 31, 1944

arbitrarily been chosen to define a survivor in contrast to the twenty-one day survival commonly used for x rays and gamma rays

With graded doses the percentage of survival of each species produced a sigmoid curve typical of the curves relating biolog-



Fig 4 Gross effects of total surface irradiation with beta rays on rats, exposed to 5 000 rep on Oct 28 1944

ical effects with dose of ionizing radiations. As shown in Figure 6, the critical dosage ranges, as measured in air at the surface of

the animal, varied roughly as the size of the animal. The median lethal dose, or LD50, for each species, the dose required to

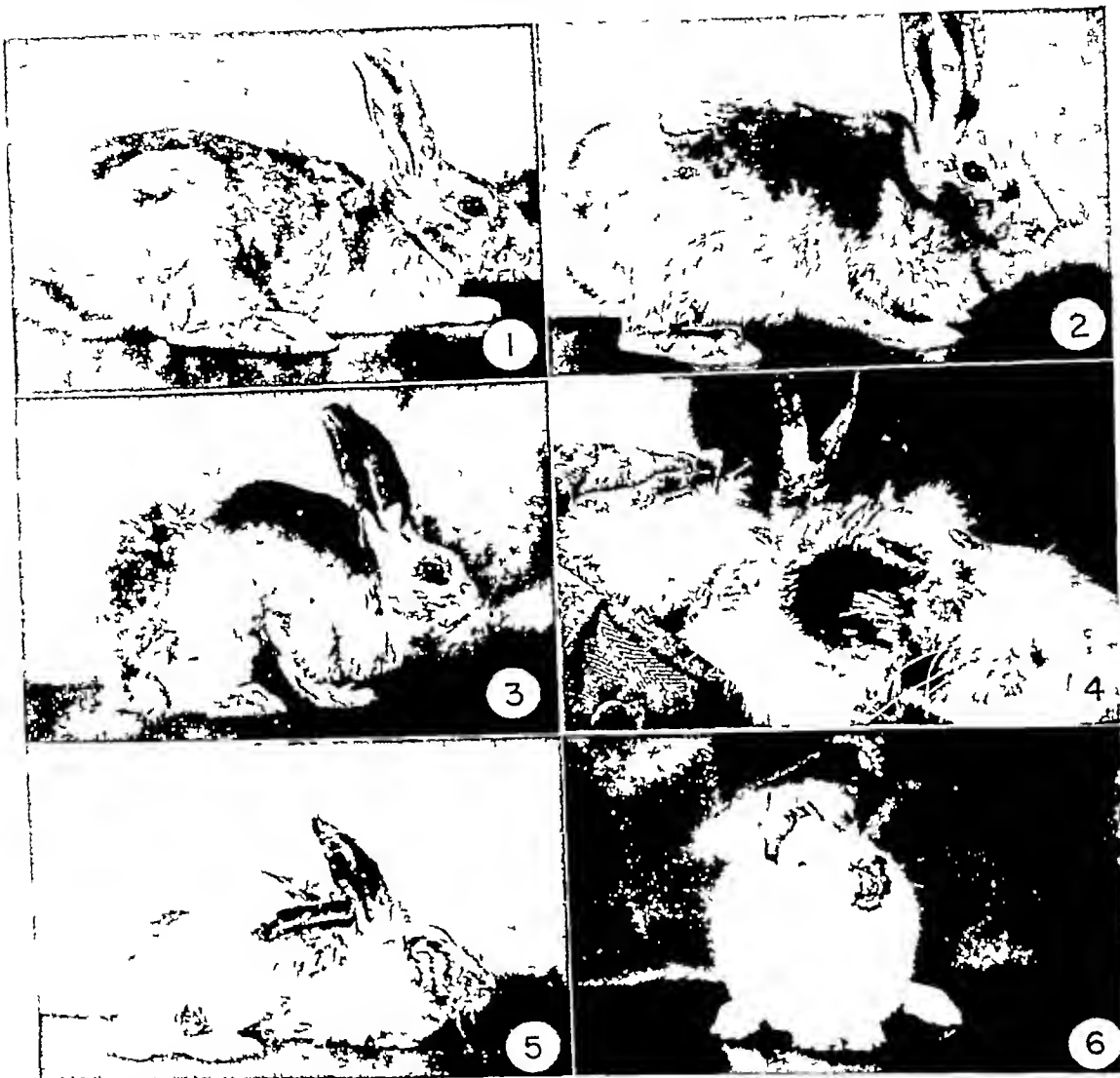


Fig 5 Gross effects of total surface irradiation with beta rays on rabbits the doses and incubation periods are as follows 1 3,000 rep, 10 weeks 2 5 000 rep, 10 weeks 3 7 500 rep, 10 weeks 4 15 000 rep, 7 weeks 5 15 000 rep 11 weeks 6 25 000 rep, 19 days

kill 50 per cent of the animals within forty-five days after exposure, was found to be as follows

Baby rats	2,200 rep
Mice	4,700 rep
Rats	7,500 rep
Guinea pigs	7 750 rep
Rabbits	c 17,000 rep

Baby rats	510 r
Mice	840 r
Rats	1,280 r
Guinea pigs	310 r
Rabbits	1,500 r

For comparison with beta rays, survival studies were performed with gamma rays on each of the five different species, and the median lethal doses which were established are as follows

The lethal action of beta rays must necessarily be brought about by an over-all mechanism which differs at least in detail from that of death induced by penetrating radiations, since all of the energy of the beta rays is absorbed in a superficial layer of tissue whose mass is small relative to the total mass of the animal Further analysis of comparative lethal effects of external

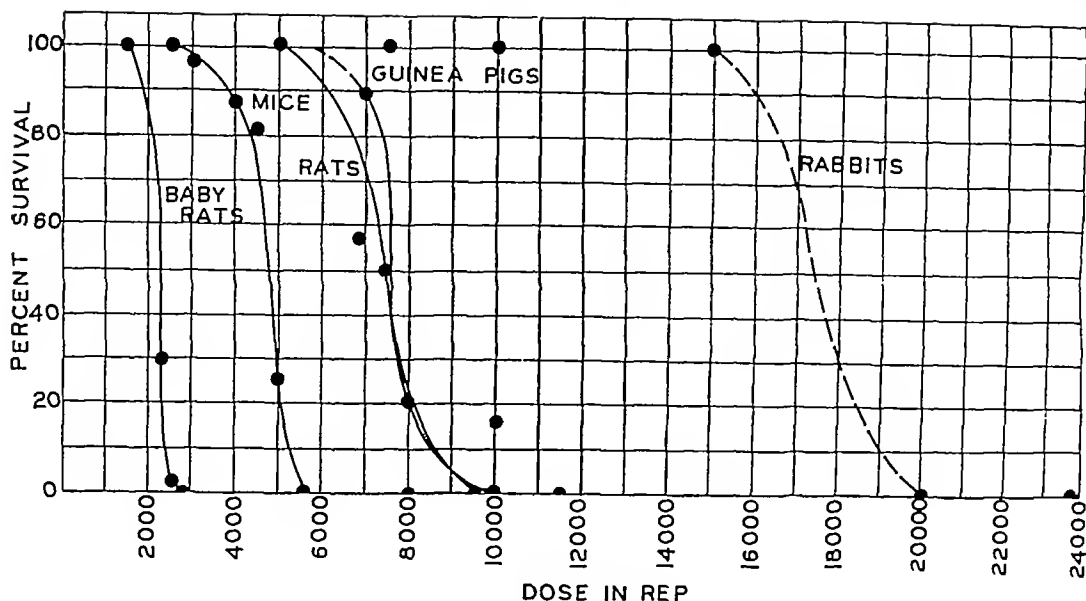


Fig. 6 Survival curves following graded doses of beta rays administered to the entire body surface

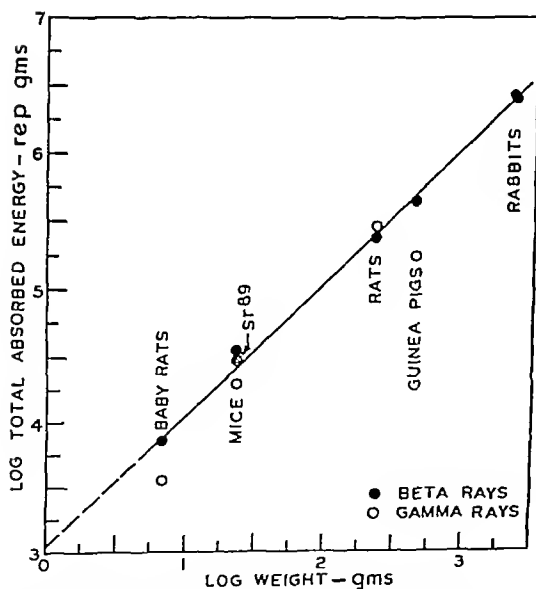


Fig. 7 Relation of animal weight and total absorbed energy as beta rays and gamma rays required to kill 50 per cent of exposed individuals

beta irradiation on a series of animals varying greatly in size and a comparison between beta-induced effects and those produced by penetrating radiations indicate a number of relationships of some interest

Such analysis and comparison can be made only if the various doses of beta rays and γ - or gamma rays are reduced to

equivalent units of energy absorbed. The unit chosen is the gm rep, or that amount of radiant energy absorbed in a gram of tissue to give a uniform dose of one roentgen equivalent physical, or 83 ergs.

The total amount of gamma ray energy absorbed to produce 50 per cent killing is simply the product of the median lethal dose, in r, times the weight of the animal in grams. The total amount of energy absorbed as beta rays to produce the same effect is given by the product of the median lethal dose in rep times the surface area of the animal in square centimeters divided by the absorption coefficient of the particular beta emission used.

The total beta/total gamma ratios for killing in the various species varied from 0.84 in the rat to 3.24 in the guinea-pig. Interestingly enough, these ratio values for the different animals varied as their respective sensitivities to gamma rays or inversely as their gamma ray median lethal doses. Thus it was indicated that beta rays, a strictly superficially absorbed radiation, bring about their lethal action by a total mass or volume effect, while gamma rays, which irradiate all elements of the body more or less uniformly, do not.

For beta rays this relation may be ex-

pressed the total energy absorbed to produce 50 per cent killing is directly proportional to the weight of the animal. The accuracy of this relationship is tested in Figure 7 where the log total energy of beta rays in gm rep (ordinates) is plotted against the log average weight of the animal species studied (abscissae).² The survival of mice following graded doses of beta rays from strontium⁸⁹ indicated total energy absorption for 50 per cent killing in very close agreement with the predicted value. This would seem to have significance in view of the appreciably lower average energy of the beta emission of strontium⁸⁹ than that of phosphorus³² used in the extended series. For comparison with beta rays comparable points for gamma rays are included in this graph. The total absorbed energies of gamma rays required to produce 50 per cent killing show a general proportionality with size, but two of the points, those for baby rats and guinea-pigs, have values much less than half those required to satisfy the relationship established for beta rays.

Acute doses of beta rays below the critical lethal range also have a marked effect on the longevity of animals. This relationship has been worked out only in the case of mice, since only with this species have enough individuals been irradiated to furnish reliable data. In Figure 8 is shown the relationship between dose of external beta rays and the time required for 50 per cent of the animals to die. Two different mechanisms are apparently involved (1) acute radiation death, in which changes in dose have negligible effect on the time of death, (2) delayed death brought about probably through reduced resistance and by infection of skin lesions. In the latter case, the time of death is strongly affected by variations in the administered dose.

A series of preliminary experiments were performed to determine the rate and pattern of recovery from total surface beta irradiation in mice. In this study the split-dose technic was applied to recovery

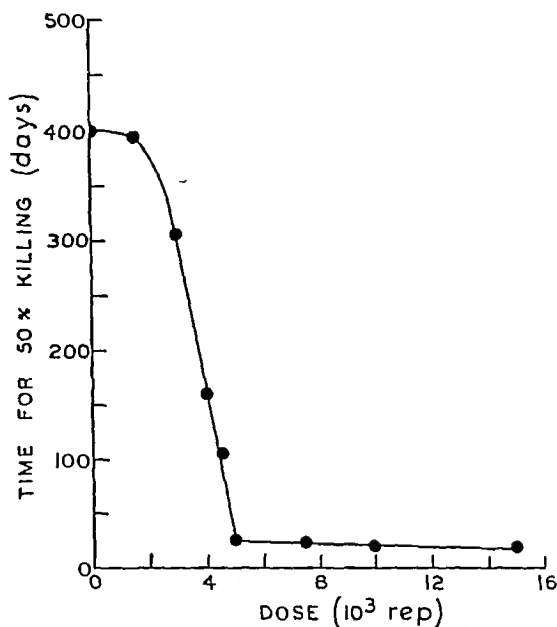


Fig 8 Effect of dose of beta rays on the time of survival of mice

as tested by lethal effects. A conditioning dose of 3,000 rep, the greatest dose which would result in no killing within forty-five days after irradiation, was followed at various time intervals up to sixteen weeks by graded test doses of beta rays. The variation in total dose required to produce 50 per cent killing at the different time intervals gave a measure of the recovery which had occurred between the conditioning and the test doses.

The resulting survival curves for each of the different time intervals are shown in Figure 9. At each split-dose interval the total median lethal dose is significantly greater than that for a single exposure, 4,700 rep. When the recovery at each time interval is calculated and plotted against time, the resulting curve gives the pattern of recovery from potentially lethal damage (Fig 10).

Recovery is at first very rapid, two-thirds of the effectiveness of the conditioning dose having been lost at the end of the third day and complete recovery having been attained by the end of the eighth day. Beyond the eighth day there is an over-compensation, that is, test doses greater than the standard LD50 (4,700 rep) are

² This relationship extrapolated to an animal the size of man would indicate a median lethal surface dose of about 60,000 rep of beta rays.

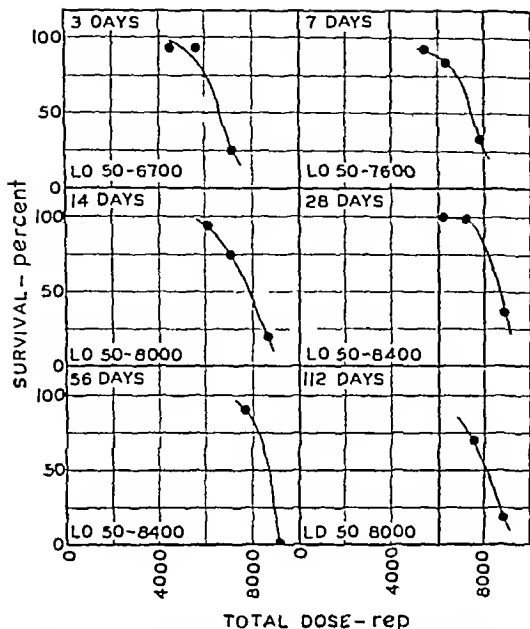


Fig 9 Survival of mice following divided doses of beta rays. Survival values given obtain at forty-five days after the second exposure

required to kill 50 per cent of the animals within forty-five days. A maximum recovery of 123 per cent is reached at forty days, and thereafter there is a loss of recovery, falling to 110 per cent at one hundred and twelve days.

There is no obvious explanation of this over-recovery. Histological studies have shown a marked thickening of the skin following a single dose of beta rays, but such thickening is only apparent four to five weeks after irradiation, whereas the over-compensation begins as early as eight days after exposure.

Another approach toward an elucidation of the mechanism of beta-ray lethal action has been through the determination of the degree of additivity of the radiobiological effects of beta and gamma irradiation in mice. The lethal studies, briefly described above, would indicate that the mechanisms of lethal action of the two radiations have at least some common features. Furthermore, a number of recent papers have shown that the effect of different ionizing radiations are completely additive in producing certain biological effects, provided the energy absorption distribution of the two

radiations is comparable. Irradiation of mice with both beta rays and gamma rays was indicated as a means of determining the effect of major differences in the locale of direct tissue damage.

A number of preliminary experiments in which the exposures to the two radiations were made at different times (a maximum

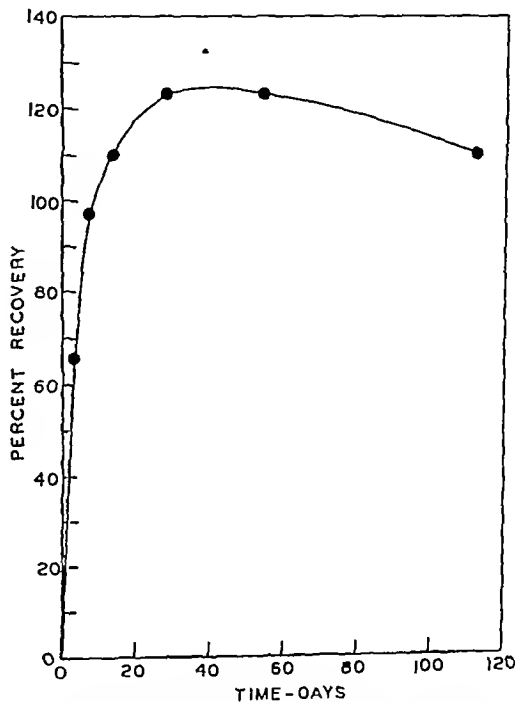


Fig 10 Recovery from radiation damage in mice following exposure to beta rays as measured by the lethal effect.

of a few hours apart) gave inconclusive results. In these cases it was apparent that recovery from damage inflicted by the first administered radiation was appreciable but, unfortunately, adequate data for the proper correction for recovery was unavailable. A subsequent series, in which the two radiations were administered simultaneously, thereby avoiding the problem of recovery, demonstrated definite additivity.

On the basis of absorbed energy, the lethal studies described above showed that in mice gamma rays are 1.75 times as effective in producing lethal action as beta rays. Since the survival curves for the two radia-

tions are very similar, it is possible to establish a standard base curve which represents the expected survival for any combination of added doses of beta rays and gamma rays assuming that their effects are completely additive. From the standard base curve a zero additivity curve can be constructed for dosages of beta and gamma rays in any proportion by plotting added dose, in effectiveness units, against the product of the percentage surviving each dose separately. A plot of observed sur-

Blood studies on rabbits which received total surface irradiation with beta rays, in doses ranging from 1,500 rep to 59,000 rep, revealed no direct effect on the cellular constituents of peripheral blood. Sporadic increases of heterophils beginning three weeks after irradiation with intermediate doses, 10,000 and 15,000 rep, coincided with severe infection of ulcerated skin. No evidence of indirect effect on white blood cells was found nor was there any evidence to substantiate the claim of lymphocyte

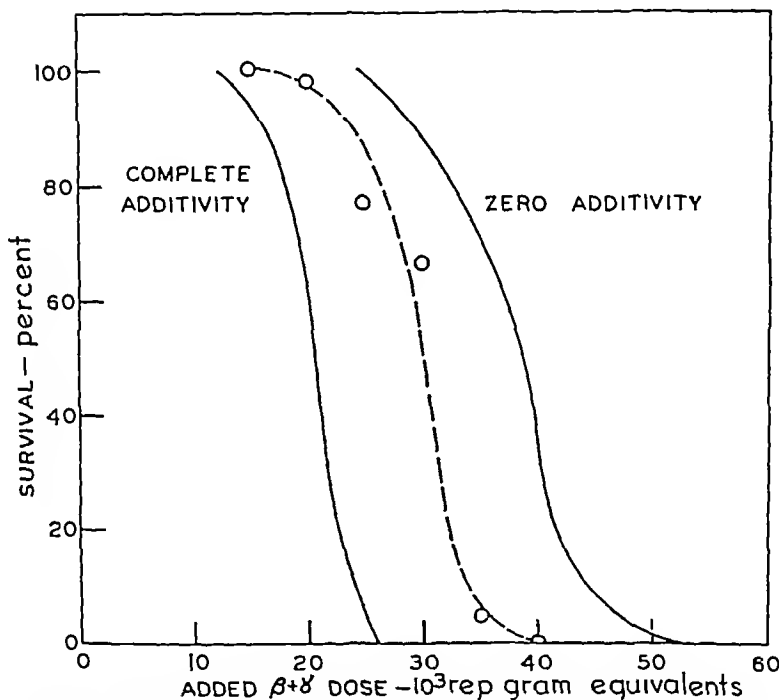


Fig 11 Survival of mice following simultaneously added doses of beta rays and gamma rays. Doses are given in an effectiveness ratio of $1\beta/1\gamma$.

vivals against such curve pairs constitutes a sensitive test for additivity.

In Figure 11 the percentage survival in each of six groups of 24 mice (ordinates) is plotted against added dose of beta and gamma rays in effectiveness units (abscissae) along with the complete and zero additivity curves. The best curve drawn through these experimental points falls almost precisely halfway between the two test curves and indicates 50 per cent additivity of the effects of the two radiations in causing lethal action in mice.

stimulation by superficial irradiation. The lack of effect of beta irradiation on the peripheral blood is considered to be consistent with the physical properties of the radiation and the anatomical features of the rabbit.

Single sublethal total surface doses of beta rays induced the formation of tumors in significant incidence in mice and rats, but produced none in either guinea-pigs or rabbits. Tumor induction was particularly striking in the case of rats (Sprague-Dawley albinos) at doses of 4,000 and 5,000

rep All of the animals exposed to these doses of beta rays developed a great multiplicity of tumors belonging to practically every type of skin abnormality known, but with this Dr Henshaw's paper will deal in more detail (see p 349)

Many of the experiments performed to determine the effect of total surface beta

irradiation were exploratory in nature and none can be considered as totally adequate, but they do give, I think, the general pattern of effects and point the way for more elaborate and carefully controlled work in the future

Botany Department
University of Chicago
Chicago 37, Ill

SUMARIO

Efectos de la Irradiación Beta Superficial Total

Par virtud de su absorción superficial los rayos beta a dosis inferiores a la esca'a letal aguda producen mayores lesiones macroscópicas y superficiales en los animales de laboratorio, que los rayos X más penetrantes y que los gamma En los ratones, ratas y conejos provocaron oclusión de los ojos, depilación y úlceras, pero en su localización la depilación y ulceración tomaron una forma típicamente distinta en cada especie La principal onda de mortalidad sobrevino algo más tarde que después de la irradiación con rayos X o gamma La dosis letal media (DL50) varió toscamente conforme al tamaño del animal de 2,200 ref (roentgens equivalentes físicos) en las ratillas a 17,000 ref en los conejos

Una comparación de la dosis letal media de rayos beta y gamma reveló que la razón de beta total/gamma total en las diversas especies variaba en proporción directa a su respectiva sensibilidad a los rayos gamma o inversa a la dosis letal media de rayos gamma para la especie dada, indicando que los rayos beta, con su radiación absorbida absolutamente en la superficie, ejercen su acción letal por un efecto total en masa o volumen, en tanto que los rayos gamma, que irradian más o menos por igual todos los elementos de cuerpo, no actúan así

Los estudios de la longevidad en los ratones mostraron que los cambios de dosis ejercían poco efecto en lo referente a muerte aguda por irradiación, pero sí afectaban intensamente el momento de la muerte tardía, debido, presuntamente, a la menor resistencia e infección de las lesiones cutáneas

Los experimentos preliminares con una técnica de dosis dividida para determinar la velocidad y forma de la reposición en los ratones después de administrar una dosis de acondicionamiento, reveló que la reposición era rápida al principio y completa al cumplirse el octavo día, desde cuya fecha se observaba hipercompensación, es decir, que se necesitaban dosis de ensayo superiores a la DL50 establecida para dicha especie (4,700 ref) para matar a 50 por ciento de los animales en término de 45 días

La aditividad del efecto radiobiológico de los rayos beta y gamma en su acción letal sobre los ratones resultó ser de 50 por ciento

Los estudios ejecutados en los conejos no revelaron efecto alguno de los rayos beta superficiales totales sobre los elementos de la sangre periférica Evocaron oncogenia en los ratones y ratas, pero no en los conejos o cobayos

The Metabolism of the Fission Products and the Heaviest Elements¹

JOS G HAMILTON, M D

Division of Medical Physics (Berkeley), Divisions of Medicine and Radiology (San Francisco)

University of California

AN INVESTIGATION of the assimilation, distribution, retention, and excretion of fission products and the heaviest elements in the rat has been conducted at the Crocker Radiation Laboratory of the University of California. These studies were initiated Oct 15, 1942, and are continuing at the present time. An extensive survey has been made of the metabolism of twenty different radio-elements. This project has been carried forward by Dorothy Axelrod, M A, Asst Prof D H Copp, M D, Ph D, Josephine Crowley, A B, Harvey Fisher, A B, Ph D, Henry Lanz, Jr, A B, Kenneth G Scott, A B, L Van Middlesworth, Ph D, and the author. During the early phases of the work, we were fortunate in having the advice and aid of Professors I L Chalkoff, D M Greenberg, and their associates, who assisted the program materially, particularly in the studies with strontium, barium, and cesium. Also with the group, during the war, were Assoc Prof Roy Overstreet and Asst Prof Louis Jacobson, whose contributions included the radiochemical preparations necessary for the tracer studies. We acknowledge with gratitude the facilities that were extended to us by Prof Ernest O Lawrence to do this work in the Radiation Laboratory, the constant advice and encouragement given to us by Dr Robert S Stone and his colleagues of the Health Division in the Plutonium Project, the assistance and counsel from Dean S L Warren and his staff, the help of the operating crew of the 60-inch cyclotron for the preparation of most of the radio-

elements used in these studies, and the cooperation of Profs W M Latimer, G T Seaborg, and their associates in providing certain key radio-elements for these studies, notably neptunium, plutonium, americium, and curium.

INTRODUCTION AND METHODS

During the early phases of the development of the Plutonium Project, it became apparent that one of the most serious problems to be encountered was the protection of personnel working in this field against the immense quantities of radiation and radioactive materials produced by the chain-reacting pile. The most important hazard that arises from the release of nuclear energy are radiations produced directly from fission and subsequently emitted by the resultant fission products and plutonium. The fission products can produce injury either as an external source of radiation or, if they gain entry into the body, by acting as an internal radioactive poison, quite analogous to radium poisoning. This latter consideration is a major concern, since the amounts required within the body to produce injurious effects are minute compared to the quantities necessary to induce damage by external beta and gamma irradiation.

A comparison with the history of the radium industry gives an index of the magnitude of the problem presented by fission products and plutonium to the medical protection program of the Plutonium Project. A total of approximately one kilogram of radium has been isolated since its discovery fifty years ago. During this

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interval, a large number of instances of radium poisoning have been recorded which arose from working with what now seems to be, by comparison, a trifling amount of radioactivity. The chain-reacting piles at Hanford have produced kilogram quantities of plutonium which had to be isolated and purified by a very elaborate and complicated series of chemical processes. At the same time, a comparable mass of fission products was created, in the piles, and the amount of radioactivity from these fission products with moderately long half-lives was in the range of hundreds of megacuries. Thus, one can see the magnitude of the problem as presented in relation to possible poisoning from fission products and, of course, plutonium.

The fission of uranium results in the production of thirty-four radioactive elements, extending from zinc to europium, and there have been identified nearly two hundred radioactive isotopes of this large number of elements that arise from fission. Since the possibility of entry of these fission products into the body had to be considered as one of the principal hazards to those working in the field of atomic energy, it was necessary to secure information as to the absorption, distribution, retention, and excretion of these radioactive materials. In addition to evaluating the metabolic characteristics of these substances, it was necessary to duplicate as nearly as possible, with laboratory animals, the manner by which fission product poisoning might occur. This included a study of the behavior of these radioelements following their introduction into the body by the three major portals of entry, namely inhalation, oral ingestion, and through cuts and abrasions of the intact skin.

Another point, aside from the problem of the quantities of the fission products, was the fact that knowledge had to be obtained concerning the behavior of a large number of different substances whose patterns of metabolism differ not only from radium, but from one another. No

satisfactory estimates or predictions of the possible metabolic characteristics of most of the fission products could be made, since most of these substances are radioactive isotopes of elements concerning whose metabolic properties very little was known. In other words, there were no reliable data available that could make it possible in most instances to predict which of the fission products would be absorbed from the digestive tract and rapidly eliminated, once having gained entry into the body, and which ones might be selectively deposited and retained in some vital structure. Actually, there was only one fission product, radioiodine, that had received sufficient study with regard to its metabolic properties, prior to 1942, to permit a reasonable evaluation of the amount that could be tolerated within the body without producing damage (1). A second fission product, radiostrontium, had been studied before 1942 (2, 3), but not in sufficient detail to satisfy the requirements of the medical research program of the Plutonium Project. The nature of the metabolic characteristics of the other fission products at that date was essentially a completely unknown quantity.

The radioactive isotopes of these fission product elements were individually prepared and in the carrier-free² state (4). This latter precaution, which rendered considerably more difficult the preparation of these materials, was necessary since the fission products arise in the carrier-free state in the chain-reacting pile and it was deemed essential that the specific activities of the materials employed in the tracer experiments at Berkeley be comparable to the specific activities of the fission products that might be encountered by workers in the Plutonium Project. The fission products prepared, isolated, and subjected to metabolic study included strontium, yttrium, zirconium, columbium, ruthenium, tellurium, iodine, xenon, cesium, barium, lanthanum, cerium, praseo-

² The term carrier free signifies that the radioelement was not diluted with measurable quantities of the stable non radioactive form of the same element.

dymium, and element 61³ Currently, these studies are being extended to include some of the less abundant fission products, notably arsenic, technetium (element 43), silver, cadmium, indium, tin, and antimony Later, it is planned to complete the investigation of the entire list of fission products Those fission products selected for the experiments described in this paper were restricted to the radio-elements that occur in greatest abundance from fission and which have relatively long half-lives

In addition to the fission products, it was necessary to evaluate by similar tracer studies the potential dangers from plutonium poisoning This element is radioactive and has a half-life only fifteen times greater than radium In addition, the quantities to be isolated, purified, and used for a variety of purposes were considerable, to say the least Later, several other of the heaviest elements, commonly called the actinide elements, which extend from actinium through curium (element 96) were included for study These substances either arise directly in the chain-reacting pile or appear in certain phases of the atomic energy program and present potential health hazards because they all share the common property of radioactivity The members of this group subjected to metabolic study at Berkeley to date include thorium, protoactinium, neptunium (element 93), americium (element 95), and curium Tracer studies with uranium were done elsewhere (5, 6) As has been emphasized in the preceding paragraphs, it is obvious that the first step in the evaluation of the hazard to health presented by the possible entry into the body of both the fission products and the actinide elements was to study their metabolism

The tracer studies have included a survey of the metabolism of the fission products and plutonium in the rat following oral ingestion, inhalation, and parenteral injection The absorption, distri-

bution, retention, and excretion were investigated for each substance Extensive radioautographic studies were made of those organs in which a high degree of selective localization took place in order that a correlation could be made between the accumulation of the radio-element with the microscopic anatomy of the tissue The experimental animals employed for the tracer studies were adult male and female rats The radio-chemically pure and carrier-free individual fission products and plutonium were administered by parenteral injection, stomach tube, and intratracheal intubation in solutions of isotonic sodium chloride The quantity of radioactivity administered to each animal was in the range of from 0.5 to 5.0 microcuries This was done to avoid as much as possible any radiation effects that might have altered the normal metabolic state of the experimental animals

The rats were maintained in specially designed metabolism cages so that the feces and urine could be collected separately at daily intervals The animals were sacrificed in groups of from three to nine at varying intervals after administration of the different radio-elements The usual time intervals were one, four, sixteen, and sixty-four days, although in some instances a few of the studies were less extensive, but in the case of plutonium, not only were the time intervals extended to nearly one year, but tracer experiments were made of this element in each of its principal three valence states, namely, plus 3, plus 4, and plus 6 Twelve to fifteen organs and tissues were removed and their radioactivity determined as well as the fraction eliminated in the excreta

The pulmonary intubation studies, which were somewhat qualitative in character, were extended by a series of aerosol experiments A number of successful procedures were developed and employed for the production of stable aerosols of the carrier-free mixture of fission products and plutonium in both soluble and insoluble forms Rats were exposed to these

³ Element 61 which does not exist in a known stable form in nature was prepared at the Clinton Laboratories Oak Ridge Tenn

TABLE I METABOLISM OF THE PRINCIPAL MEMBERS OF THE LONG-LIVED FISSION PRODUCTS AND CERTAIN OF THE HEAVIEST ELEMENTS IN MAN AND THE RAT FOLLOWING PARENTERAL AND ORAL ADMINISTRATION

Radio-Element	Half Life (S)	Fission Yield (S)	Oral Absorption	Accumulation in Principal Organs of Retention	Rate of Elimination from Principal Organs of Retention (Half time in the Body)	
Strontium						
Sr ⁸⁹	53 D	4 6%	5-60%	65% Bone	Bone	>200 D
Sr ⁹⁰	25 Y		5-60%	65%, Bone	Bone	>200 D
Barium						
Ba ¹⁴⁰	12 8 D	6 1%	5-60%	65%, Bone	Bone	> 50 D
Iodine						
I ¹³¹ *	8 0 D	2 8%	100%	30% Thyroid	Thyroid	> 30 D
Cesium						
Cs ¹³⁵	33 Y		100%	45%, Muscle	Muscle	15 D
Yttrium						
Y ⁹¹	57 D	5 9%	<0 05%	65%, Bone	Bone	>500 D
Lanthanum						
La ¹⁴⁰	40 H	6 1%	<0 05%	{65%, Liver 25%, Bone	{Liver Bone	{10 D > 25 D
Cerium						
Ce ¹⁴¹	28D	5 7%	<0 05%	55% Liver	Liver	10 D
Ce ¹⁴⁴	275 D	5 3%	<0 05%	25% Bone	Bone	>200 D
Praseodymium						
Pr ¹⁴³	13 8 D	5 4%	<0 5%	{30% Liver 40% Bone	{Liver Bone	{10 D >100 D
Element 61						
61 ¹⁴⁷	3 7 Y	2 6%	<0 05%	{50% Liver 30% Bone	{Liver Bone	{10 D >100 D
Zirconium						
Zr ⁹⁵	65 D	6 4%	<0 05%	45% Bone	Bone	>100 D
Columbium						
Cb ⁹⁵	37 D	6 4%	<0 5%	{40% Bone 25% Blood	{Bone Blood	{30 D 1 D
Ruthenium						
Ru ¹⁰³	42 D	3 7%	<0 05%	3 5% Kidney	Kidney	20 D
Ru ¹⁰⁶	1 Y	0 5%	<0 05%	3 5% Kidney	Kidney	20 D
Tellurium						
Te ¹²⁷	90 D	0 033%	25%	15% Blood	Blood	15 D
Te ¹²⁹	32 D	0 19%	25%	6% Kidney	Kidney	15 D
Thorium						
Th ²³⁴	24 5 D		<0 05%	50% Bone	Bone	>200 D
Protoactinium						
Pa ³¹	3 × 10 ⁴ Y		<0 05%	40%, Bone	Bone	>100 D
Neptunium						
Np ²³⁹	2 2 D		<0 05%	60% Bone	Bone	> 50 D
Plutonium						
Pu ²³⁹	2 2 × 10 ⁴ Y		0 007%	65% Bone	Bone	> 2 Y
Americium						
Am ²⁴¹	500 Y		<0 05%	{70% Liver 25% Bone	{Liver Bone	{10 D > 1 Y
Curium						
Cm ²⁴²	150 D		<0 05%	{70% Liver 25% Bone	{Liver Bone	{10 D > 1 Y
Xenon						
Xe ¹³³	5 3 D	4 5%	Distribution proportional to fat content of body, half time in the body two hours			

* Human studies (1) † Human studies (9)

radioactive aerosols, and their absorption, distribution, retention, and excretion were followed for varying intervals extending for nearly a year (7). Radioautographic preparations were made of pulmonary tissue in both the intubation and aerosol studies.

In addition to the experiments outlined above, tracer studies were done following the parenteral and oral administration of thorium, protoactinium, neptunium, americium, and curium. Here, the time intervals ranged from one day to nearly a year.

RESULTS

The most important metabolic characteristics of the fission products and several of the actinide elements studied are listed in Table I. It is seen that most of the fission products and all of the actinide elements included there are not absorbed to a significant degree by way of the digestive tract. Following parenteral administration, they are accumulated in the skeleton, and eliminated from this organ very slowly. Only five of the listed fission products are absorbed from the digestive tract to a significant degree, notably

strontium, barium, tellurium, iodine, and cesium Xenon is readily and rapidly absorbed through the lungs following inhalation and is as readily eliminated from the lungs Strontium and barium are deposited and retained to a high degree by the skeleton Iodine is accumulated

tribution of strontium, barium, tellurium, iodine, and cesium, following oral absorption, is indistinguishable from their metabolism after parenteral administration With the exception of ruthenium, the remainder of the fission product series and all of the actinide elements listed in Table

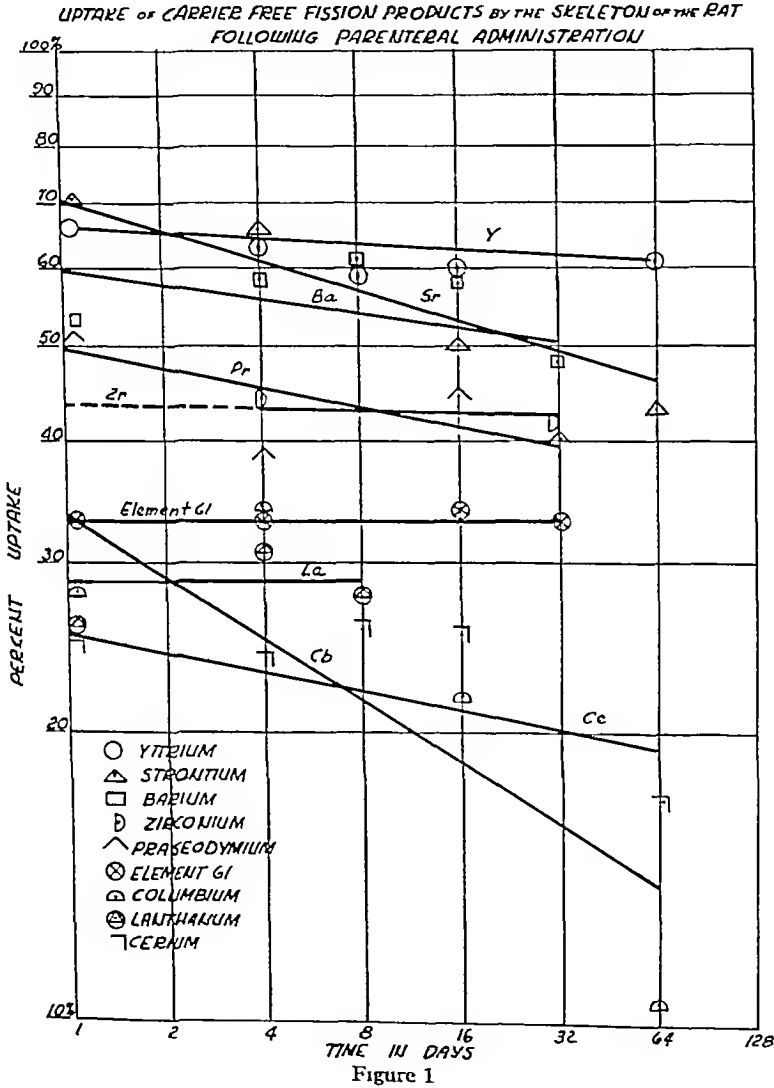


Figure 1

and retained by the thyroid Tellurium shows some accumulation in the kidneys and blood, with a rather rapid rate of release from these tissues Cesium is distributed quite uniformly throughout all of the tissues, the greatest accumulation occurring in the muscle, and it is quite promptly excreted The pattern of dis-

I show a high degree of accumulation and prolonged retention by the skeleton as shown in Figures 1 and 2 In the case of lanthanum, cerium, praseodymium, element 61, americium, and curium, there is an initially high degree of accumulation by the liver, but they are quite rapidly excreted from this organ, presumably by

way of the bile (Figs 3 and 4) Except for the liver, the content in the soft tissues was relatively small following the parenteral administration of the fission product and actinide elements that are accumulated in the skeleton After one month the spleen and kidney usually had the highest

their rates of radioactive decay The long-lived fission products that fall into this category include Sr^{89} , Y^{91} , Zr^{95} , Ba^{140} , La^{140} , Ce^{141} , and Pr^{143} With the exception of iodine in the thyroid, the remainder of the fission products listed in Table I, namely Ru^{103} , Ru^{106} , Te^{127} ,

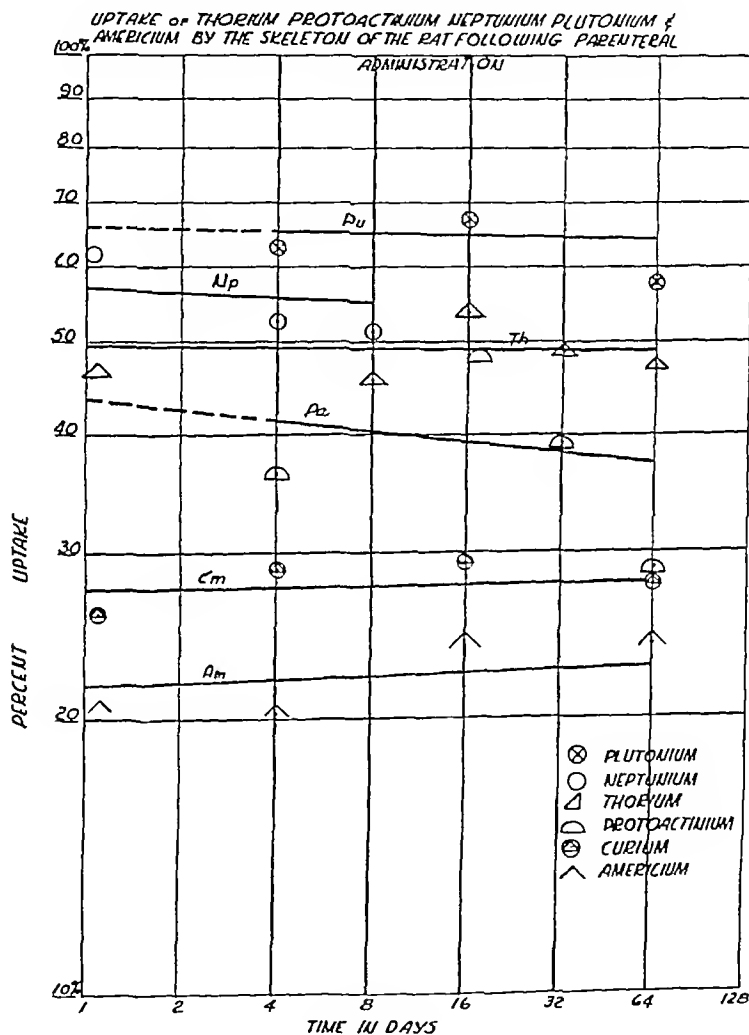


Figure 2

concentration per gram unit weight, which ranged from one-tenth to one-quarter that of bone after two months or more

It will be noted in Table I that, with the exception of Cb^{93} , and possibly Sr^{90} , Ce^{144} , and Gd^{147} , the rates of elimination of the different fission products that are accumulated in the skeleton are less than

Te^{129} , Xe^{133} , and Cs^{135} , are rapidly excreted and at rates greater than their half-lives

The rates of elimination from the skeleton of the actinide elements listed in Table I are very slow and, in the case of plutonium, the excretion in the rat falls to 0.01 per cent per day of the amount re-

maining in the body within a year following the intramuscular administration of this radioactive element. The metabolism of plutonium following intramuscular injection is the same after the administration of this element as Pu^{3+} , Pu^{4+} , and Pu^{6+} . This indicates that plutonium is con-

of undecalcified rat femurs (10). The metabolism of strontium in the skeleton is very similar to calcium and, as might be expected, the radioautographs revealed that the accumulated radiostrontium in the femur was quite evenly distributed throughout the mineral structure of the

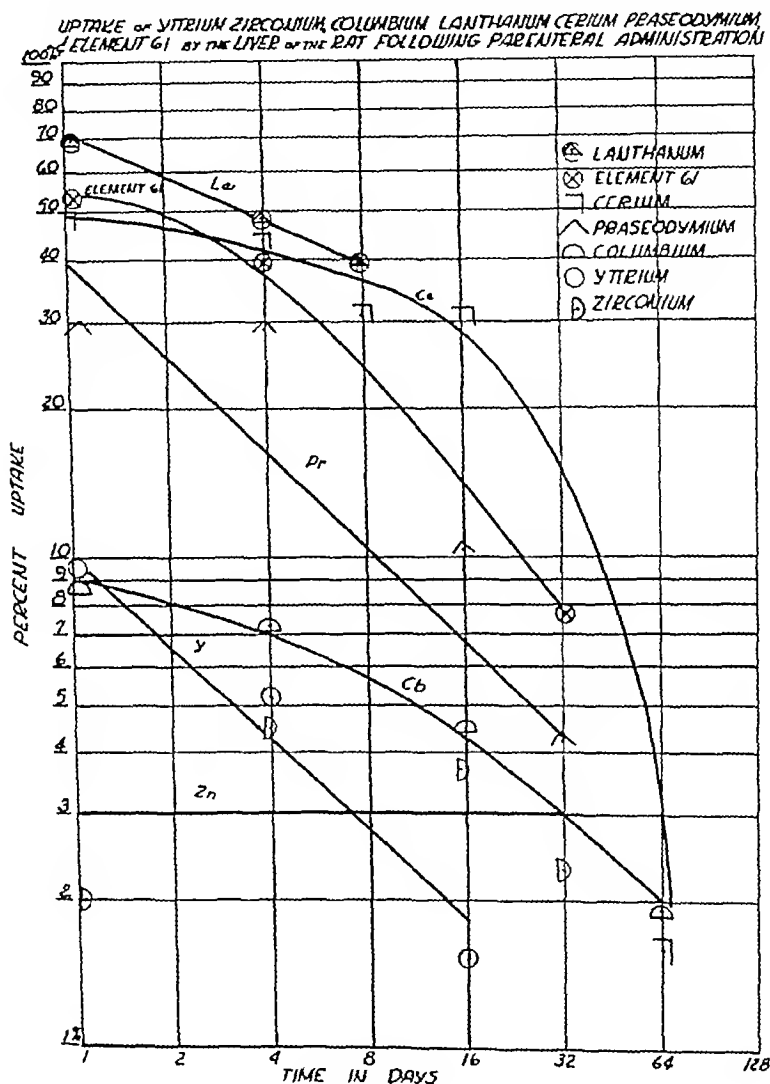


Figure 3

verted by the body to one valence state regardless of the valence of this element when administered. Considerable evidence has been accumulated to indicate that plutonium in the body is tetravalent.

Radioautographic studies were made of the distribution of Sr^{90} , Y^{89} , Zr^{90} , Ce^{144} , Th^{233} , Pu^{239} , and Am^{241} in 5-micron sections

bone (Fig 5). The other radio-elements studied by this technic showed a startling deviation from the pattern of distribution of the radiostrontium. Plutonium exhibits this phenomenon to a marked degree, and in Figures 6 and 7 it can be seen that most of this element is deposited in the periosteum, endosteum, and in the

way of the bile (Figs 3 and 4) Except for the liver, the content in the soft tissues was relatively small following the parenteral administration of the fission product and actinide elements that are accumulated in the skeleton After one month the spleen and kidney usually had the highest

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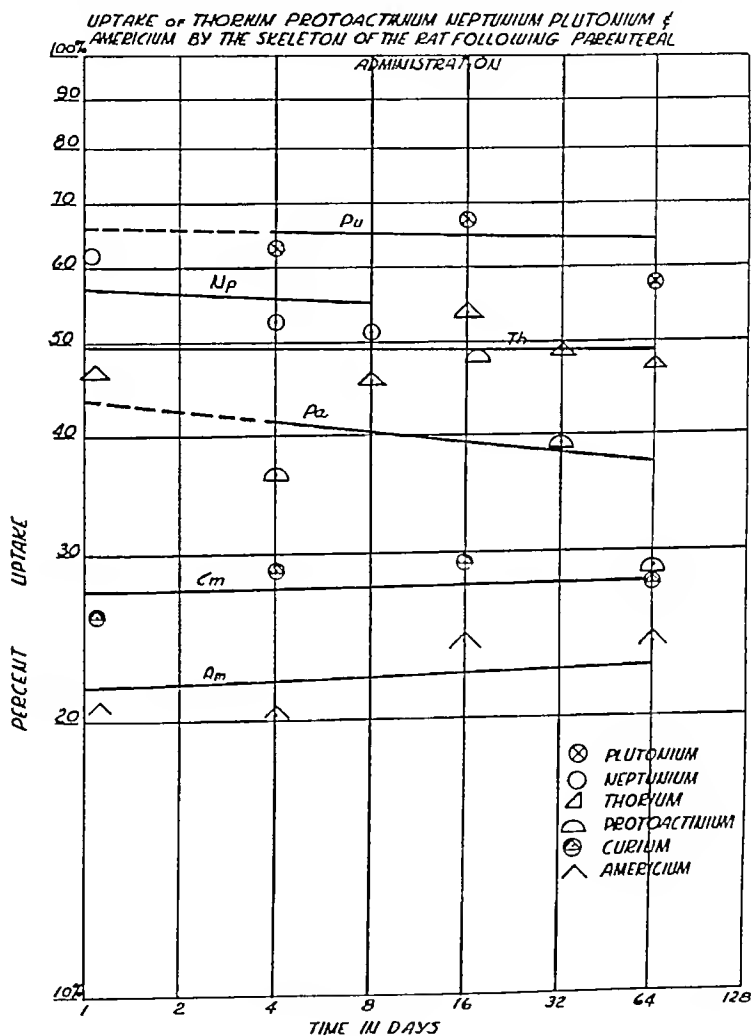


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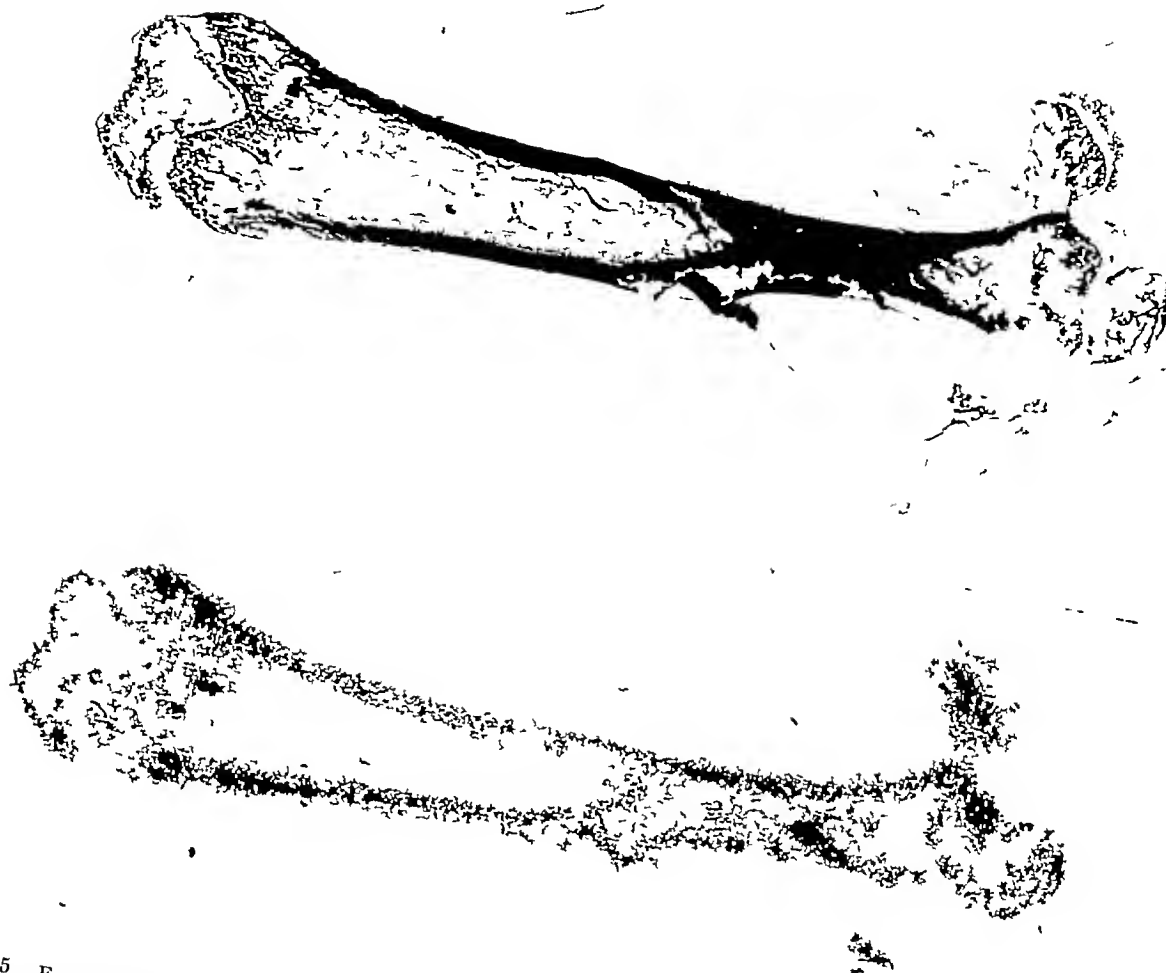


Fig 5 Femur from rat weaned to control diet at three weeks injected with 5 microcuries of radioactive strontium intraperitoneally at five weeks and sacrificed one week later Note even deposition of radioactive strontium throughout the mineral bone and deposition in the calcifying trabeculae beneath the epiphyseal plate AgNO₃ hematoxylin and eosin $\times 6$

The direct introduction into the lungs of solutions of the carrier-free fission products and plutonium showed that those radio-elements that were not absorbed from the digestive tract were retained by the lungs to a considerable degree and for a prolonged period of time. The fission products that were deposited and retained by the lungs included yttrium, zirconium, columbium, ruthenium, plutonium, cerium, and praseodymium. Plutonium also showed a high degree of retention by the pulmonary tissue, which

was greatest for Pu⁴⁺ and least for Pu⁶⁺. Radioautographs indicated that the deposited radio-elements were distributed throughout the lungs in the alveoli. No accumulation in the bronchial tree, lymph nodes, or blood vessels was noted, even after several months. Some absorption took place through the lungs for all of the substances retained by the lungs and, except for ruthenium, most of the absorbed material was deposited in the skeleton, as would be expected from the parenteral metabolic studies. Those fis-

region of the trabecular bone. These results suggest that the plutonium in the trabecular structure is not incorporated in the bone but rather is deposited in the covering of the trabeculae. The distribution in bone of yttrium, zirconium, cerium, thorium, and americium resembles

shown in Figures 10 and 11. It is thought that the material may be in the walls of the small blood vessels of the bone.

These studies suggest that accumulation of this group of radio-elements occurs principally in the osteoid matrix. The pattern of distribution does not appear

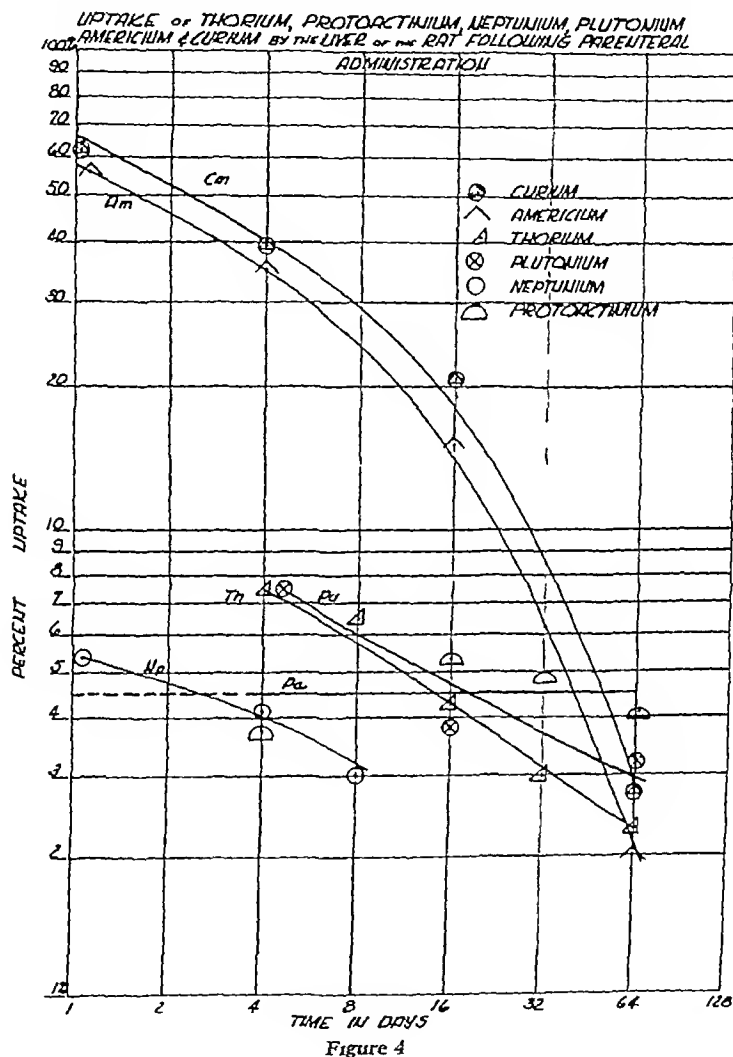


Figure 4

the pattern seen with plutonium with a few minor variations. A radioautograph of thorium is shown in Figure 8 and a zirconium radioautograph in Figure 9. Some accumulation of a very spotty character occurs in the cortex with cerium and americium, and representative bone radioautographs of cerium and americium are

to change significantly with time. Radioautographs from adult rats that had received plutonium nearly a year before they were sacrificed showed no essential difference in the distribution of that radioelement in the bone from studies in which the animals were sacrificed a few days after its administration.

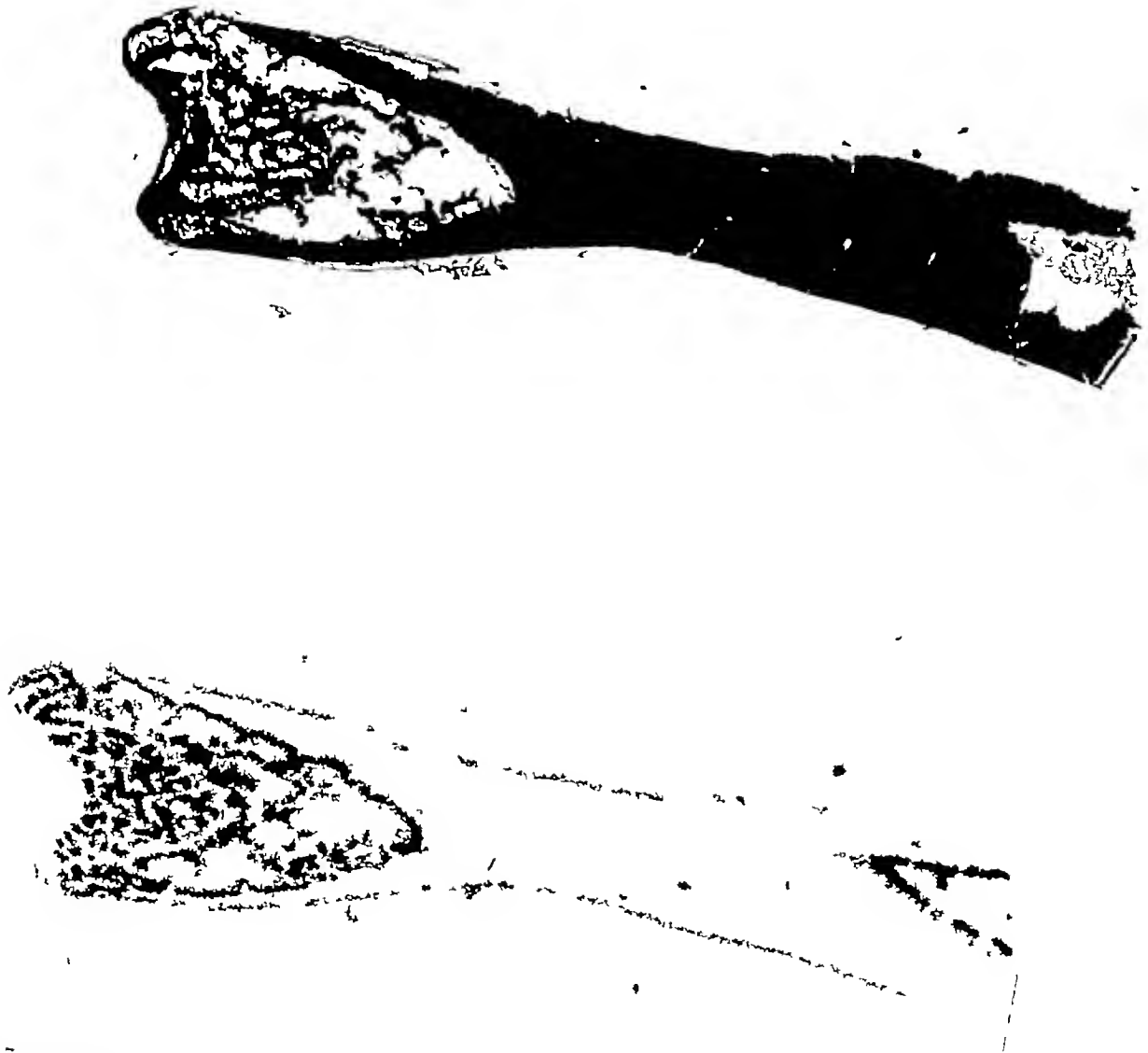


Fig 7 Femur from adult rat injected with 15 micrograms of plutonium and sacrificed at eight weeks. Note the superficial deposition of plutonium in the periosteum endosteum and region of trabecular bone and the absence of activity from the bone marrow. $\text{Ag}\backslash\text{O}_2$ hematoxylin and eosin $\times 9$

cated that the fission product mixture and plutonium aerosols were composed principally of particles ranging in diameter from 0.5 micron to 0.1 micron. Approximately 75 per cent of the material inhaled was retained in the rat. The retention was divided almost equally between the lungs and the upper respiratory tract. The material in the upper respiratory tract was rapidly removed, presumably



Fig 6 Femur from adult rat (10-12 months old) injected with plutonium and sacrificed one week later. Note the superficial deposition of plutonium in the surface of the shaft and trabeculae and the absence of plutonium from the epiphyseal cartilage. AgNO_3 , hematoxylin and eosin. $\times 14$

sion products that are absorbed through the digestive tract, notably strontium, barium, tellurium, iodine, and cesium, were found to be readily absorbed through the lungs

These experiments, which were rather qualitative in character, were later followed by a large series of aerosol studies (7). An examination of particle sizes by means of the electron microscope indi-



Fig 7 Femur from adult rat injected with 15 micrograms of plutonium and sacrificed at eight weeks. Note the superficial deposition of plutonium in the periosteum, endosteum, and region of trabecular bone, and the absence of activity from the bone marrow. AgNO_3 , hematoxylin, and eosin. $\times 9$

cated that the fission product mixture and plutonium aerosols were composed principally of particles ranging in diameter from 0.5 micron to 0.1 micron. Approximately 75 per cent of the material inhaled was retained in the rat. The retention was divided almost equally between the lungs and the upper respiratory tract. The material in the upper respiratory tract was rapidly removed, presumably

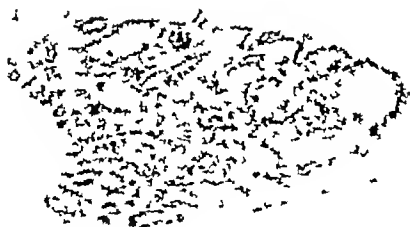
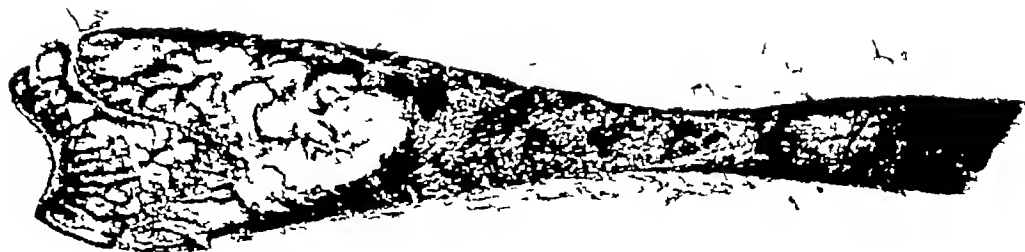


Fig 8 Femur from adult rat injected with 32 microcuries of thorium and sacrificed after eight days Note the similarity to plutonium AgNO_3 hematoxylin and eosin $\times 7$

by ciliary action, and appeared in the feces. The fraction remaining in the lungs was eliminated quite slowly. Eight months after exposure to a PuO_2 aerosol, 4 per cent of the total quantity inhaled still remained in the lungs. Comparable values were observed with aerosols of $\text{PuO}_2(\text{NO}_3)_2$ and the long-lived fission products. There was very little absorption from the lungs and subsequent deposition

in the skeleton following the inhalation of the PuO_2 and the fission product aerosols in an insoluble form. However, nearly 10 per cent of the plutonium, when inhaled as an aerosol of $\text{PuO}_2(\text{NO}_3)_2$, was absorbed through the lungs in the first twenty-four hours and deposited in the skeleton. Little absorption occurred after the first day. From the qualitative data obtained by the tracheal intubation



Fig 9 Femur from adult rat injected with 10 microcuries of zirconium and sacrificed at twenty one days
 Note the similarity to plutonium AgNO_3 , hematoxylin, and eosin $\times 8$

studies with the individual fission products and the $\text{PuO}_2(\text{NO}_3)_2$ aerosol experiments, it appears probable that the inhalation of aerosols of soluble compounds of all the fission products and the actinide elements would result in at least some absorption from the lungs

Radioautographs of pulmonary tissue from the aerosol studies (Fig 12) revealed that, immediately after inhalation, the

active material was deposited in both the bronchial tree and the air sacs. Within one day the material in the bronchial tree vanished (Fig 13), presumably it was moved out by ciliary action and swallowed in the sputum. The large fraction remaining in the lungs was quite evenly distributed throughout the alveoli, and the pattern of distribution showed little change with time. The slow and continued re-

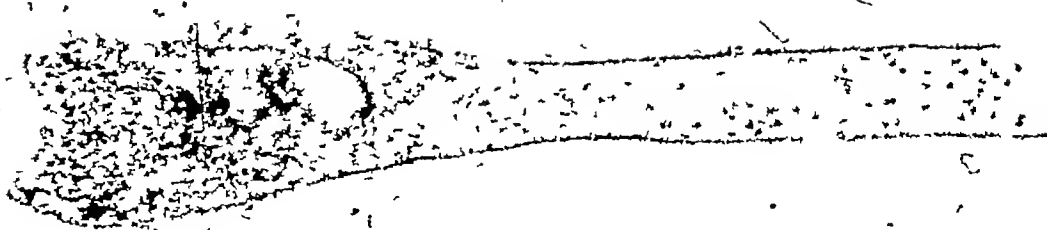


Fig 10 Femur from adult rat injected with 10 microcuries of cerium and sacrificed at eight days. Note similarity to americium (Fig 11) AgNO_3 hematoxylin and eosin $\times 7$

DISCUSSION

lease of active material from the alveoli probably also took place primarily by way of the bronchial tree. This deduction is based on the observation that the fecal excretion of plutonium and the fission product mixture closely corresponded to the elimination of these materials from the lungs.

The most interesting aspect of the results obtained from this work are the metabolic patterns observed of the fission products and actinide elements following parenteral administration. Here we see the response of the animal organism to extremely minute traces of a series of di-

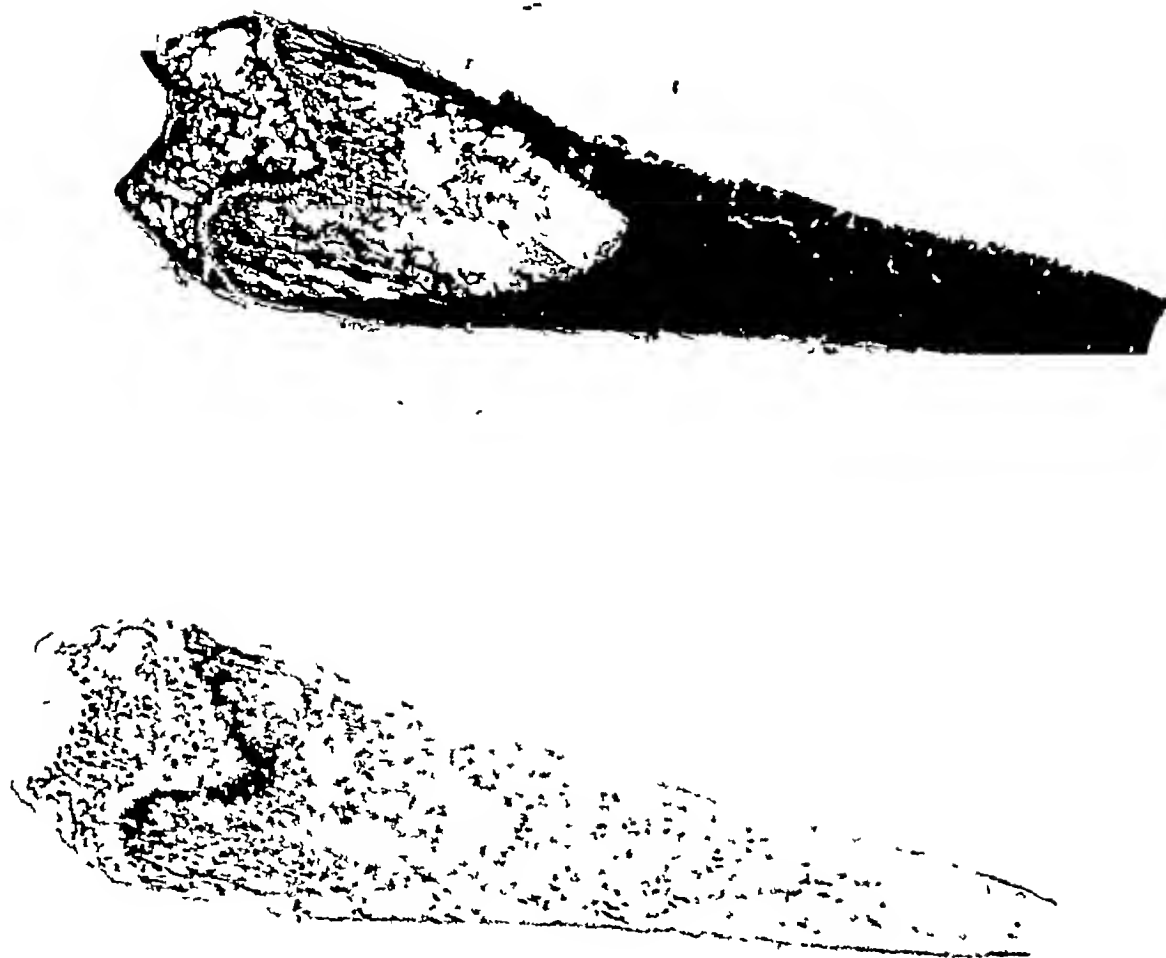


Fig 11 Femur from adult rat injected with 8 micrograms of americium and sacrificed at sixteen days. Note the spotty distribution of the element in the shaft and the heavy deposition in areas of bone trabeculae. AgNO_3 , hematoxylin and eosin $\times 8$

ferent elements. The majority of the elements investigated either are not normally present in the body in detectable quantities, or they are new elements not existing in nature and which have been made by artificial means. Substances studied that fall into the latter group are element 61, neptunium, plutonium, americium, and curium.

Space does not permit a discussion of a number of the unusual results obtained from these experiments. The surprising predilection of many of the long-life fission products and the actinide elements for prompt deposition and prolonged retention in the skeleton is noteworthy. A closer study of this phenomenon has brought to light information of both



Fig. 12 Lung from rat sacrificed immediately after inhalation of aerosol of plutonium oxide. Note plutonium deposition on the walls of bronchi and bronchioles and throughout the alveolar structure. Note the absence of plutonium from blood vessels. Hematoxylin and eosin. $\times 8$.

academic and practical importance. As has been already pointed out, all of these radioactive elements that accumulate in

bone and were subjected to radiographic study, with the exception of strontium, are not deposited in the mine

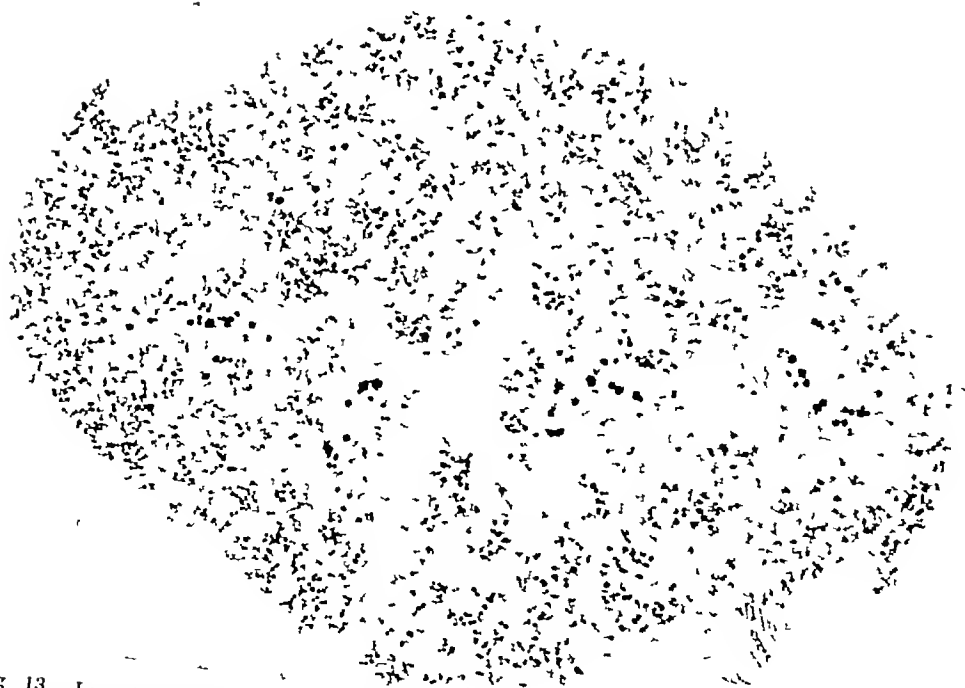
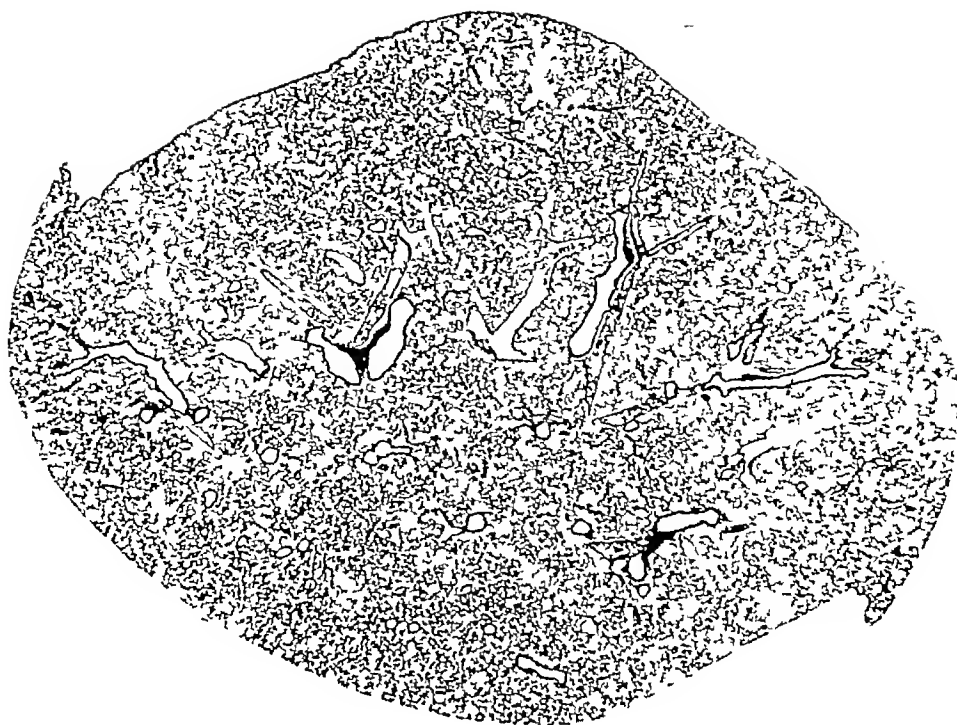


Fig 13 Lung from rat sacrificed one day after inhalation of an aerosol of plutonium oxide. Plutonium has disappeared from the bronchial surfaces but large amounts are distributed throughout the alveolar structure. Hematoxylin and eosin $\times 8$

structure of bone, but rather appear to be localized in and adjacent to the osteoid matrix. To date, this behavior has been observed to occur with yttrium, zirconium, cerium, thorium, plutonium, and americium. In view of certain similarities of chemical properties, together with related metabolic characteristics, it seems likely that comparable patterns of histological distribution in the bone will be encountered with lanthanum, praseodymium, neodymium, element 61, samarium, europium, actinium, neptunium, and curium. Very possibly the same phenomenon will be observed with columbium and protoactinium.

The large fraction of lanthanum, cerium, praseodymium, element 61, americium, and curium deposited in the liver was an unexpected finding. This effect was apparently not due to accumulation of these radio-elements by the reticulo-endothelial system, since the uptake per gram in the spleen ranged from 1/40 to 1/70 of the maximum concentration in the liver. Moreover, the rapid excretion from the liver is evidence against the deposition of these substances in the reticulo-endothelial system. The prediction can be made, on the basis of the close similarity of chemical properties, that the high level of uptake by the liver will be also observed with neodymium, samarium, and europium.

Obviously much work yet remains to be done before speculations such as these can be transformed into established facts.

The practical aspect of the unique behavior of these fission product and actinide elements that are deposited in bone is worthy of considerable attention. In the first place, with the possible exception of columbium, all of these substances accumulated in bone are released at a very slow rate. This, of course, places them in the category of radium in so far as retention in the skeleton is concerned. Some of them, particularly most fission products, have half-lives very much shorter than that of radium, and they emit beta particles instead of alpha particles.

This reduces somewhat their hazardous nature, but these factors are only quantitative, not qualitative. The majority of the actinide series possess the undesirable characteristics of radium in that they have both long half-lives and emit alpha particles. In addition, a number of the fission product and actinide elements have been shown to possess the curious property of accumulating in the region of the osteoid matrix and it is predicted that more of these elements will demonstrate the same effect. As a result of this phenomenon, radiations emitted from such substances can enter the marrow cavity most effectively, since these elements are laid down in a thin layer of tissue adjacent to it. This situation is particularly serious for those materials which emit alpha particles, because a large proportion of all disintegrations will result in the bombardment of the radiosensitive bone marrow. Radium can be predicted to be considerably less of a menace for comparable amounts of radioactivity than, for example, plutonium, for it is presumably distributed throughout the mineral structure of the skeleton with the result that most of the radium alpha particles are absorbed within the apatite structure of the bone and only a small fraction of the total number of disintegrations can escape to irradiate the blood-forming tissues.

Radiation Laboratory
University of California
Berkeley 4 Calif

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SUMARIO

El Metabolismo de los Productos de Fisión y los Elementos Pesados

Como primer tiempo en las justipreciación del riesgo que entraña para la salud la entrada, en el cuerpo, por varias vías, de las sustancias radioactivas producidas por la pila de reacciones en cadena, ejecutáronse en las ratas estudios metabólicos en relación con los productos de fisión y del plutonio y ciertos otros de los elementos más pesados o actínidas

Ni la mayor parte de los productos de fisión ni ninguno de los elementos actínidas fueron absorbidos en mayor grado por vía digestiva, aunque se acumularon en el esqueleto, del cual fueron eliminados con mucha lentitud. Obtuvieronse autorradiografías de varios de los radioelementos, observándose que, con excepción del es-

troncio, se depositaban principalmente en la matriz osteoidea y junto a la misma, más bien que en la porción mineral del hueso. Esta situación reviste mayor gravedad con respecto a las sustancias que emiten partículas alfa, dado que una gran proporción de todas las desintegraciones darán por resultado el bombardeo de la radiosensible médula ósea.

Varios de los elementos radioactivos se depositaron en el hígado en cantidades considerables, pero este efecto aparentemente no se debía a acumulación por el aparato retículo-endotelial, observación esta comprobada por la rápida excreción de dichas sustancias por el aparato mencionado.

Histological Changes Following Radiation Exposures¹

WILLIAM BLOOM, M D

University of Chicago

OUR GROUP, which consisted of Drs Murray, DeBruyn, Pierce, and Snider, Miss Rhoades, Miss Heller, my wife, and, for part of the time, Drs Block, Conway, Jacobson, and Lisco, examined large series of animals, exposed to a variety of external and internal sources of radiation α -rays, fast and slow neutrons, gamma rays from radium and from the Clinton pile, beta rays from the external phosphorus source mentioned previously in this Symposium, and internally administered radium, plutonium, sodium²⁴, phosphorus³², barium¹⁴⁰, lanthanum¹⁴⁰, strontium⁸⁹, radio zirconium, yttrium⁹¹, and in a few instances radio cerium. The work was done under the general direction of Dr R S Stone and was carried out in the laboratories supervised by Dr Kenneth S Cole in Chicago and Dr Howard J Curtis at Clinton Laboratories.

Most of our experiments were stereotyped. Animals were given the LD50/30-days dose and fractions thereof with the hope that we would find the lower limit of irradiation damage as shown by the microscope. Most of the animals used were mice and rats. There were also fair numbers of rabbits, a few guinea-pigs, and some chickens. In addition to this general type of experiment, there were several series in which animals were given repeated doses of external radiations. Two such series after gamma irradiation were produced for us by Dr Lorenz at the National Cancer Institute. Unfortunately, most of these animals have not yet been examined.

In view of the enormous literature on radiation effects during the last fifty years, it is surely unnecessary to stress the radio-sensitive in contrast to the radioresist-

ant organs. The skin, the blood-forming organs, the gonads, the gastro-intestinal tract, the thymus, are the main sites of the action of radiations. In the brief space that I have the best I can do is to discuss our general findings and to point out also a few specific histological observations.

First, irrespective of the particular external source, if the dosage was in the LD50/30-days range or in equivalent fractions thereof, we were unable to tell which type of radiation had been used on the animals. That is, given a particular animal, if it received the LD50/30-days dose, we could not tell whether it had been treated by slow or fast neutrons, α -rays, or gamma rays. We could tell, however, in the case of external beta rays because the changes were limited to the skin except in mice, where we sometimes found damage in the outer surfaces of the spleen and testes and in the ovary. As is well known, the ovary in the mouse is especially susceptible to radiation damage and with none of the radioactive materials or external radiations applied to mice have we seen greater damage to the ovary than after external beta irradiation.

After injection of the radioactive materials, the damage qualitatively was the same with all of the materials, and the same results were produced as by the external irradiations, modified only by (a) whether the materials reached a particular organ and (b) the type of particle emitted by the radioactive isotope. That is, the greater trajectory of the beta-emitting substances causes a greater range of damage from the point of focus as contrasted with alpha-emitting materials, but the types of damage produced are the

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same, irrespective of the source of external or internal irradiation. The differences are due to focalization. For instance, sodium²⁴, which is highly diffusible, gives the histological picture of total body irradiation from an external source.

Many of the radioactive materials, as Dr Hamilton has pointed out, tend to localize in bone, many of them also localize in the spleen and kidney. In the spleen and bone the effects are what we expected from irradiation in general. The kidney, we found to be exceedingly resistant, even after the accumulation of large amounts of radioactive materials in its substance. I shall return to the internally administered isotopes shortly.

In general, I would say that we found no histologic evidence for the cause of death following irradiation. That is, we could see no differences between the animals which died with an LD50/30-days dose and those which did not die after the same dose.

We were impressed by the occurrence of waves of destruction in some of the animals that received high dosages of radiation. For instance, in the rabbit there is almost complete destruction of the bone marrow after the LD50/30-days dose of x-rays, in nine days regeneration begins and may go on for a few days and then disappear again as a result of a new phase of degeneration. I have no idea why this occurs, though I understand that clinically it is a well-known phenomenon in the skin after a single dose of x-ray. One could speculate on somatic mutations but we have no evidence on this point.

I wish that we knew something about what might be called "acquired radio-resistance," of which there are suggestions in some of our animals given repeated dosages. I know hardly more about the subject than to raise the question. I think it is a fruitful field for future investigation.

As you know, there are marked species differences in the LD50/30-days dose in different animals. In general, but not always, for a particular organ the histo-

logic changes reflect the amount of radiation and not the lethal or morbid effect on the animal. For instance, in the lymphatic tissue, in the guinea-pig, after 175 r (which is roughly the LD50/30-days for our guinea-pigs), the changes in the lymph nodes were about the same as in rabbits or rats given similar doses, though the LD50 for these animals is much higher than for the guinea-pig.

It was rather difficult for us to compare the effects of our total body irradiations with most of the reports in the literature because many of the latter are based on local irradiation of a particular organ. As a result of our attempts to make this correlation, we feel fairly strongly that there is something in a total body irradiation which causes greater damage to a particular organ than localized irradiation at a much higher dosage. It is difficult to prove this, but in the few attempts at shielding that we made, and on the assumption that more recent reports in the literature give dosages comparable to the ones we were using, I feel there is a good deal of evidence for an intangible, indirect effect, though that is as far as I can go.

One of the old ideas running through the entire radiological literature is that small doses of x-rays exert a stimulating effect. This is one point on which we feel we can make some fairly definite statements. In our series, in which the dosages were cut down in the hope of finding a point where we could say definitely, "Below this point we do not find damage," we rarely found any deviation from normal with whole-body doses of x-rays below 25 r. We continued with diminishing doses below this point. If there were a primary stimulating effect, we should have seen it, and we did not. Either we found destruction or we found no difference from the control animals.

Another check on this problem was obtained with the internal sources of radiation and also the external beta rays. It has already been pointed out that external beta irradiation cause damage to the spleen, ovaries, and testes of mice

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In the case of rats, the effect of the bone-seeking isotopes is a bit different, since the rat is, for practical purposes, a continuously growing animal. In the rat the isotopes that seek bone come down not only in old bone but predominantly in the zone of new bone growth in the metaphysis, and for all practical purposes they kill this entire zone. This stops growth in length of the bone for a while, but a reparative process then sets in and eventually an entirely new epiphyseal line is produced and the bone continues to grow in length. A very early osteogenic sarcoma which developed adjacent to the dead metaphysis was found five months after the injection of strontium⁸⁹.

Zirconium, strontium⁸⁹, barium¹⁴⁰, radium, and plutonium are also deposited in large amounts in the red pulp of the spleen. From the sternum they produce secondary injury in the thymus and damage the lymph nodes severely. Many of them cause great damage to the testis and the ovary, in fact sterilizing both gonads. As mentioned above, large amounts of these materials accumulate in the kidney and apparently produce no injurious

effects there. The radioactive isotopes which are not absorbed when given by mouth produce severe damage to the intestinal tract.

Radium alone, of all the materials we studied, produced very serious calcifying arteriosclerotic changes in the walls of the blood vessels.

There is one point that we did clear up, I think, and that is the question of the sensitivity of erythroblasts. With a few exceptions, almost everyone who studied the bone marrow after irradiation seems to have avoided the question of the radiosensitivity of erythroblasts. In our material, it seemed quite obvious that the erythroblasts were exceedingly sensitive to irradiation. They are about as sensitive as the lymphocytes. We made our observations first on mammals, but it can very easily be proved in chickens. The effect of 800 r of x-rays on the bone marrow of a chicken is so marked that by the end of two hours all evidence of intravascular formation of red blood cells has been destroyed.

Department of Anatomy
University of Chicago
Chicago 37, Ill

SUMARIO

Alteraciones Histológicas Consecutivas a la Exposición a las Radiaciones

Con la esperanza de descubrir microscópicamente el límite patógeno inferior de la irradiación, efectuáronse estudios histológicos en ratones, ratas, conejos, cobayos y pollos que recibieron varias dosis de radiación. Exceptuados los rayos beta, fueron idénticos los efectos producidos por varios focos externos de irradiación: neutrones lentos y veloces, rayos X y rayos gamma. La inyección de isotopos radioactivos produjo lesiones de tipo semejante. No se descubrieron signos histológicos que indicaran la causa de la muerte consecutiva a la irradiación.

En general, pero no siempre, en un órgano dado las alteraciones histológicas

reflejaron la dosis de irradiación recibida y no el efecto letal o morbígeno sobre el animal, de modo que fué muy similar el efecto de una dosis dada sobre los ganglios linfáticos de los cobayos y conejos, aunque es muy distinta la dosis letal para las dos especies. La irradiación total del cuerpo pareció ocasionar más daño en un órgano dado que la irradiación local con una dosis mayor, pero no hay prueba absoluta de esto.

No se observaron signos de un efecto estimulante primario de la radiación, y rara vez se notaron desviaciones de lo normal con dosis de rayos X inferiores a 25 r aplicadas a todo el cuerpo.

The appearance in the spleen and testes of a zone of severe damage, a zone of lesser damage, and then a gradual transition to normal tissue was most striking. In none of this material and in none of the foci of damage about localized, internally administered radioactive isotopes did we see at the periphery of the zone of damage anything other than normal tissue. In short, if there was a primary stimulating effect of radiation, we should have seen it either with our smallest doses of externally administered radiation or about some of the foci of internal focalization.

Another idea which is widespread is that the more primitive the cell, the more susceptible it is to radiation. This may be true with some strains of cells, it is certainly not true with others. I think the first investigator to point out at least one of the flaws in this theory was Laccasagne, who studied the ovary of the rabbit. In a beautiful paper in 1913, he pointed out that in the developing ovum and its follicle the susceptibility to radiation did not mirror the youthfulness of the ovum. He found in these ovaries that sensitivity was a function of the cell strain at different times in its development, and did not depend exclusively on youth. In our work, the most striking example of radio-resistant primitive cells is the macrophage system (reticular cells). These are exceedingly resistant. In fact, I fail to recall any evidence of degenerating reticular cells in any of our animals, though the free precursors of the blood cells, which can and do develop from the reticular cells, are exceedingly susceptible to radiation injury.

It is also widely believed that mitosis is a predisposing factor toward radiation damage. The evidence for this, I think, is not at all clear. We are especially puzzled by the fact that if one examines the testis, the most sensitive cells are found to be the spermatogonia, many of which are not in mitosis at any given time, while the spermatocytes—a very high percentage of which are always dividing—are on the whole quite radioresistant. So

that mitosis—or meiosis in the case of the spermatocytes—is not, in my opinion, a predisposing factor toward radiosensitivity.

To me the most interesting point in our whole problem has been the general question of why certain strains of cells are sensitive and why others are extremely or moderately radioresistant. After more than three years' association with this project, I regret to say that I have not even a clue on which to speculate. I don't believe that it is primitiveness of cells as such, I don't believe it is mitotic activity. I find it is very difficult to understand why cells of the pancreas should be so highly radioresistant and why many cells of the intestinal tract should not be resistant.

A few words should be said about some of the radioactive isotopes. As Dr. Hamilton has shown, many of them—particularly the fission products—go to bone. Plutonium seems to have an affinity for collagenous tissue, and the matrix of bone is collagenous. I think there is a difference between the mode of entry of calcium substitutes into bone salt and the manner by which plutonium gets into bone matrix, but I believe there can be no question of the fact that plutonium gets into bone, and I agree with Dr. Hamilton that it certainly stays there.

There was a marked difference, in our experience, between mice and rats. Since we see the mice when their bones have practically ceased growing, the experiments with the radioactive isotopes in these animals would correspond fairly well to the deposition of these same substances in adult human beings. In the mice, the essential effect of the isotopes is destruction of the bone in areas in which they lodge, and of circumjacent bits of bone marrow. The beta-emitting substances like barium¹⁴⁰ and strontium⁸⁹ can completely deplete the bone marrow of a mouse. The hematopoietic function is taken over by the spleen, which normally produces a certain amount of red blood cells and granular leukocytes in these animals.

The Biologic Effects of Pile Radiations¹

P S HENSHAW, Ph.D, E F RILEY, and G E. STAPLETON

Clinton Laboratories, Oak Ridge, Tenn.

AN EXTENSIVE biological program was undertaken as a part of the Manhattan Project when it was realized that hazardous amounts of high-energy radiations would frequently be encountered during the production of plutonium and the various radioactive isotopes. The studies undertaken were directed toward a determination of biological effects such as might be encountered on the project. The most immediate need for an investigation was the provision of a more adequate experimental basis for the tolerance levels adopted to protect personnel.

Although it was considered important to determine the maximum dose of radiation which could be absorbed with impunity, it was also considered important to determine the effects produced under a wide variety of experimental conditions and, if possible, some features of the mechanism whereby these changes occurred. The latter general objective accordingly consisted of the determination of biologic effects resulting from various radiations and various types of exposure, also it included examination of results for clues indicative of the methods of radiobiologic action.

Some of the specific objectives were (1) to determine the nature of late irradiation damage in animals receiving (a) small periodic doses and (b) near lethal doses of fast and slow neutrons, gamma rays, and beta particles, (2) to determine the relative effectiveness of fast and slow neutrons and gamma rays (penetrating radiations), (3) to obtain information on thresholds and tolerance levels in animals receiving the various treatments, (4) to determine species and sex idiosyncrasies,

(5) to gather information on the mechanism of radiobiologic action.

The findings in investigations directed toward achieving these objectives were expected to be of value to future developments, such as the treatment of radiation injury, cancer therapy, the therapeutic applications of radiations to other ailments, and the use of radioactive substances in biological research.

METHODS AND MATERIALS

Radiation Sources A fast neutron may arbitrarily be described as a neutron "more likely to produce an ionization track by elastic scattering than by being captured," that is, with energies from 10^3 ev to more than 4 Mev. By the same reasoning a slow neutron may be described as one more likely to produce an ionization track by being captured than by elastic scattering, with energies less than 10^3 ev.

The fast and slow neutron studies were made by means of special carts designed to provide space for animals during treatment and facilities for intensifying and purifying the radiation to be used. For reasons of security, a description of these facilities will have to be omitted at this time. The carts, containing the animals, were wheeled into the center of the pile and were thus subjected to the action of a high neutron field. Suffice it to say that by means of the carts a field was obtained for the animals in one case which was predominantly fast neutrons and in another which was predominantly slow neutrons. In Project reports (MonH 115-117) a careful analysis is given of the nature and amount of impurities in each instance.

Fast neutrons were measured in "n,"

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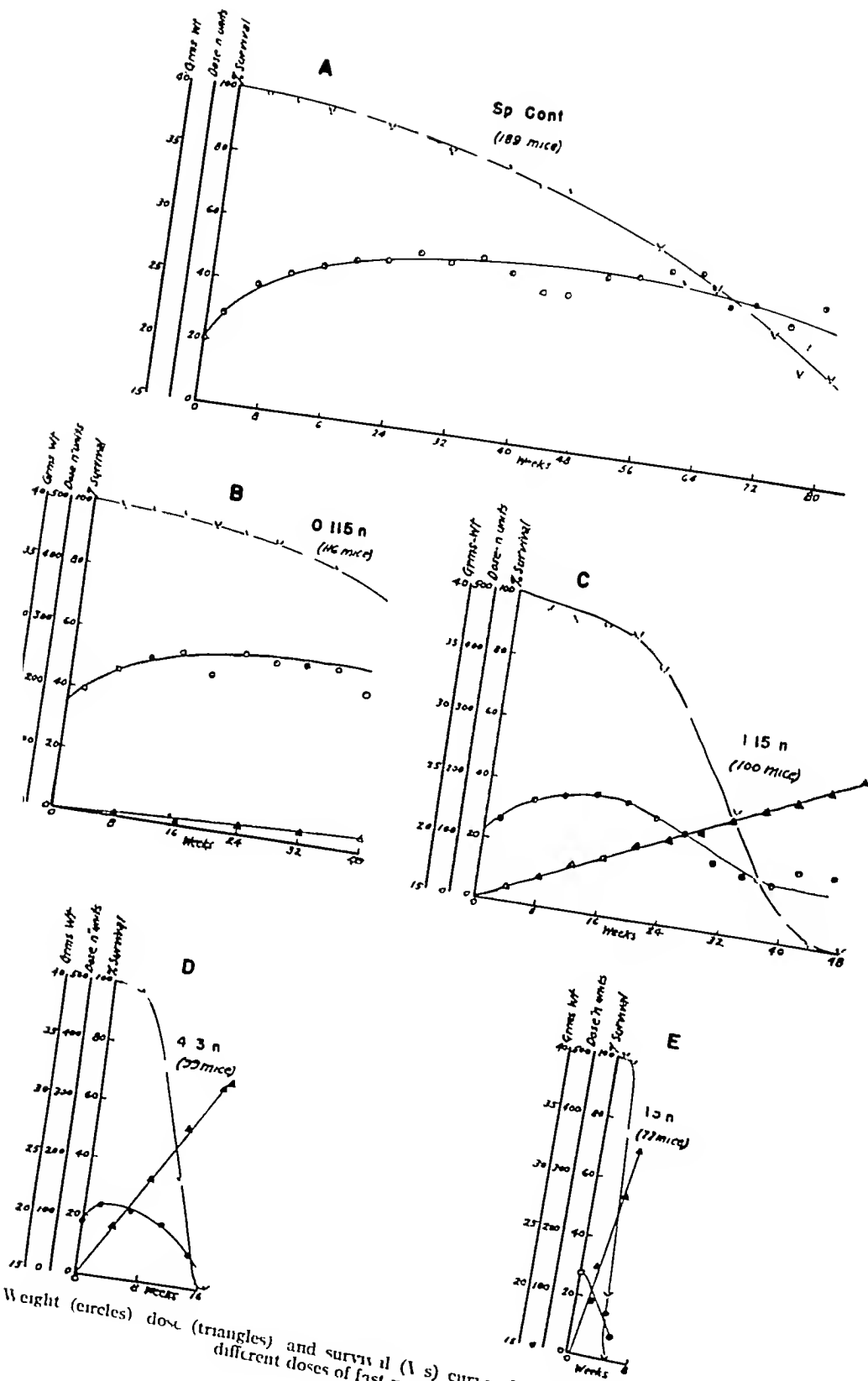
No se descubrieron datos de que la susceptibilidad a la irradiación se vincule con la juventud de la célula ni de que la carioquinesis fuera un factor predisponente a la patología debida a la irradiación

El efecto de los isotopos radioactivos fué muy distinto en los ratones y las ratas. En los ratones, en los que había cesado la osteogenia, el efecto esencial consistió en destrucción del hueso y de los fragmentos circunyacentes de médula ósea. En las ratas, en las que la osteogenia es casi continua, el isótopo se depositó predominantemente en la zona de neogenia en la metá-

fisis, con destrucción total de la zona, seguida con el tiempo de regeneración

Otros efectos nocivos de los isotopos inyectados comprendieron lesiones secundarias en el timo y ganglios linfáticos, y lesiones de los testículos y ovarios, culminando en esterilidad. No se observó patología debida a los depósitos acumulados de isotopos en los riñones. La administración oral fué seguida de lesiones gastrointestinales. El radio fué el único que produjo alteraciones arterioescleróticas en forma de calcificación. Los eritroblastos se mostraron muy radiosensibles.





the amount of ionization produced by fast neutrons which discharges a Victoreen r-meter one scale unit. The "n" values given subsequently were all obtained in this manner and corrected to be in accord with the Berkeley 100-r chamber as a standard. Slow neutrons were measured in "a" (arbitrary units, obtained with a Victoreen r-meter enclosed in a special boron-carbide box). Both the "n" and "a" values obtained, however, were converted into neutrons per square centimeter by special means which permitted more direct comparisons.

Gamma rays were obtained from a pile-activated slug of tantalum oxide. This was located within a large concrete shield with appropriate gates, in such a manner as to allow animals to be wheeled on a cart into the intense field of radiation. When the slug was properly activated, an intensity of 3 r per minute was obtained at 30 cm distance.

Beta rays were obtained from pile-activated phosphorus arranged in sheets in such a manner that animals could be enclosed within boxes of "hot" material. This radiation was measured in "rep" (roentgen equivalent physical), and accordingly beta ray doses could be compared with gamma ray doses.

Biological Materials. Mice were chosen for the experiments with penetrating radiations because they were readily available and because they could be used in statistically significant numbers despite time and space limitations. As a rule, 100 to 125 mice were used to establish the effects at any of the dose levels for the different radiations and for each sex and strain. In the case of beta rays both mice and rats were used.

Carworth CF₁ mice were chosen as the standard strain and therefore used at all the dose levels selected. Bar Harbor ABC mice were used at key dose levels to check for strain idiosyncrasies. Two special strains (A and C58 mice) were used in limited numbers to determine the effects of fast neutrons and gamma rays on animals with high lung tumor and high

leukemia incidence, respectively. Mice of both sexes were used to determine effects which might be peculiar to either sex.

The animals were handled in groups of 25, each group being kept in a separate cage which was properly marked to identify the group. Once a week the animals were placed in clean cages and checked, to be sure that all could be accounted for. All groups were weighed at intervals of one to two weeks, individual weights being obtained for certain groups. In order that progressive changes induced in the organs of the mice could be followed, animals were sacrificed at regular intervals. From at least one group of each treatment condition six mice were designated as blood-count animals by special marking. Cages were checked at least once a day, and more often twice a day, in order that all dead or moribund animals could be removed for autopsy. Records were kept of the date of death, the terminal condition of the animal, and, where possible, the cause of death.

From nearly every shipment of mice received, at least one group of 25 animals was set aside either as specific or as general controls. Those designated as specific controls received each day the same handling as the experimental mice except for exposures to radiation. Those designated as general controls were never taken from the air-conditioned animal farm. A comparison of the life span of these two types of controls served to indicate any deleterious effect other than that of radiation which affected the experimental mice.

Exposure Technique. All the radiation treatments were given in the pile building, but all other routine operations were done in the animal farm. This necessitated the daily transfer of large numbers of mice from one building to another, a distance of some 300 yards. To expedite this transfer, special cages and racks with wheels were constructed. The experimental groups and the specific control groups were kept on these racks rather than on shelves in the animal farm. The racks

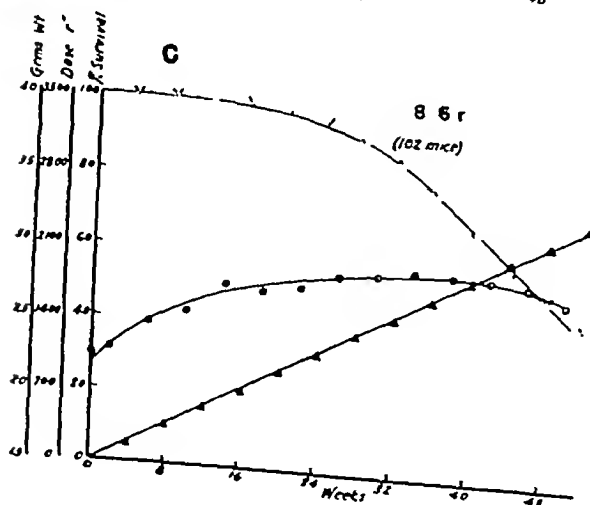
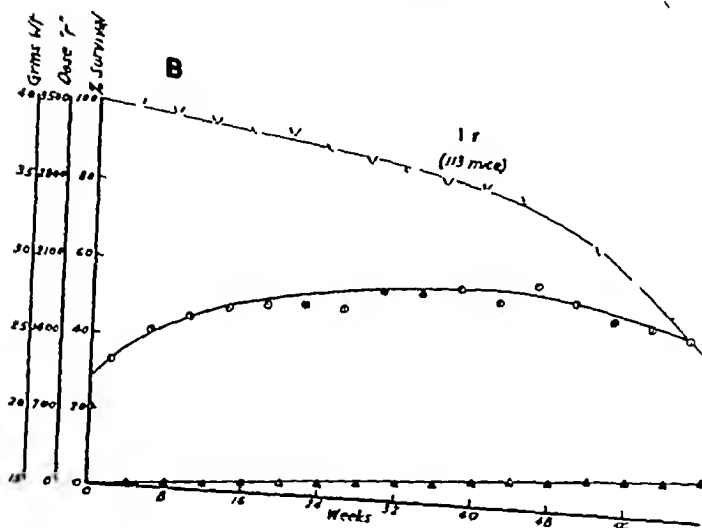
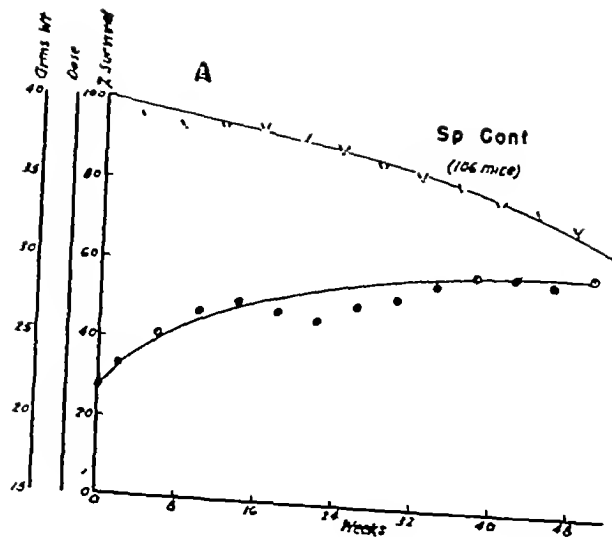


Fig 2 Weight (circles), dose (triangles) and survival (V's) curves for CF₁ female mice receiving different doses of gamma rays

were rolled onto a truck, moved to the pile building, where they were unloaded by an electric loader, and then taken by elevator to the room where the animal exposures were made

Dose Levels The program of periodic exposures was developed with the major emphasis on fast neutron rather than gamma ray exposures. Four dose levels (13, 43, 115, 0115 n) were empirically chosen for the daily fast neutron exposures. CF_1 mice, as a standard strain, were exposed at all four of these levels. Three months after the periodic fast neutron exposures were started, an evaluation of the results indicated that 115 n per day would be most useful for a study of late irradiation effects. Therefore, the 115 n per day treatment was considered to be the key dose level, and a second strain of mice, ABC, was started at this same level to check for strain peculiarities.

Although the dose levels chosen for the periodic gamma ray exposures were selected to parallel the fast neutron exposures, the limits of time and facilities did not permit the development of the complete series for gamma ray exposures. Therefore, it was decided to establish a dose level biologically equivalent to the key fast neutron dose and a second dose roughly equivalent to one-tenth this amount. Since previous experiments with massive single doses had indicated that 1 n was 7.5 times as effective as 1 r, 8.6 r per day was adopted as the key gamma dose level. Both CF_1 and ABC mice were exposed at this level. The other gamma ray dose level chosen was 10 r per day, which corresponds roughly to the lowest fast neutron level.

Criteria of Effects Weight, death, and autopsy records were obtained for all individual animals where possible. Histologic and hematologic examinations were made periodically on representative animals. Thus, in addition to having progressive weight, blood, and histologic pictures, the length of life and terminal conditions were available. Care was taken to eliminate from the final tabu-

lations records of animals killed by accident or which could not be satisfactorily autopsied.

RESULTS

Periodic Treatments (Fast Neutrons and Gamma Rays) Figure 1 shows a representative set of data for CF_1 female mice which received different daily doses of fast neutrons. Where the survival curves do not go to zero, the studies had not been completed when this paper was written. From such graphs it is possible to obtain the progressive weight changes, the time of 50 per cent survival, the accumulated dose when 50 per cent were dead, etc. At a glance it is apparent that the length of life is shortened in accord with daily exposure to fast neutrons and that the total dose when half had died was 200 to 250 n.

Figure 2 shows the results obtained with gamma rays. By means of the data in Figures 1 and 2 it was possible to obtain Figure 3, which shows per cent shortening of life as a function of fast neutron exposure in n. By placing the point representing the percentage shortening of life caused by 8.6 r of gamma rays, one obtains a ratio of effectiveness of the two kinds of radiation. It would appear then that 0.25 n and 8.6 r have the same effect, or that the effectiveness ratio is 1 to approximately 35. This is very different from the 1 to 7.5 ratio for acute killing of mice, which furnished the basis for selecting the 115 n and 8.6 r dosage values for use.

The data available do not show a precise threshold dosage value for the shortening of life, but for CF_1 mice as used, it appears to be approximately 1 r and something less than 0.1 n.

Hematologic changes for the most part were absent in animals receiving doses of 115 n or 8.6 r or less per day. Irradiation effects on the blood picture in this strain of animals are, however, somewhat obscured by the fact that the leukocyte level drifts downward with age.

No significant differences were observed

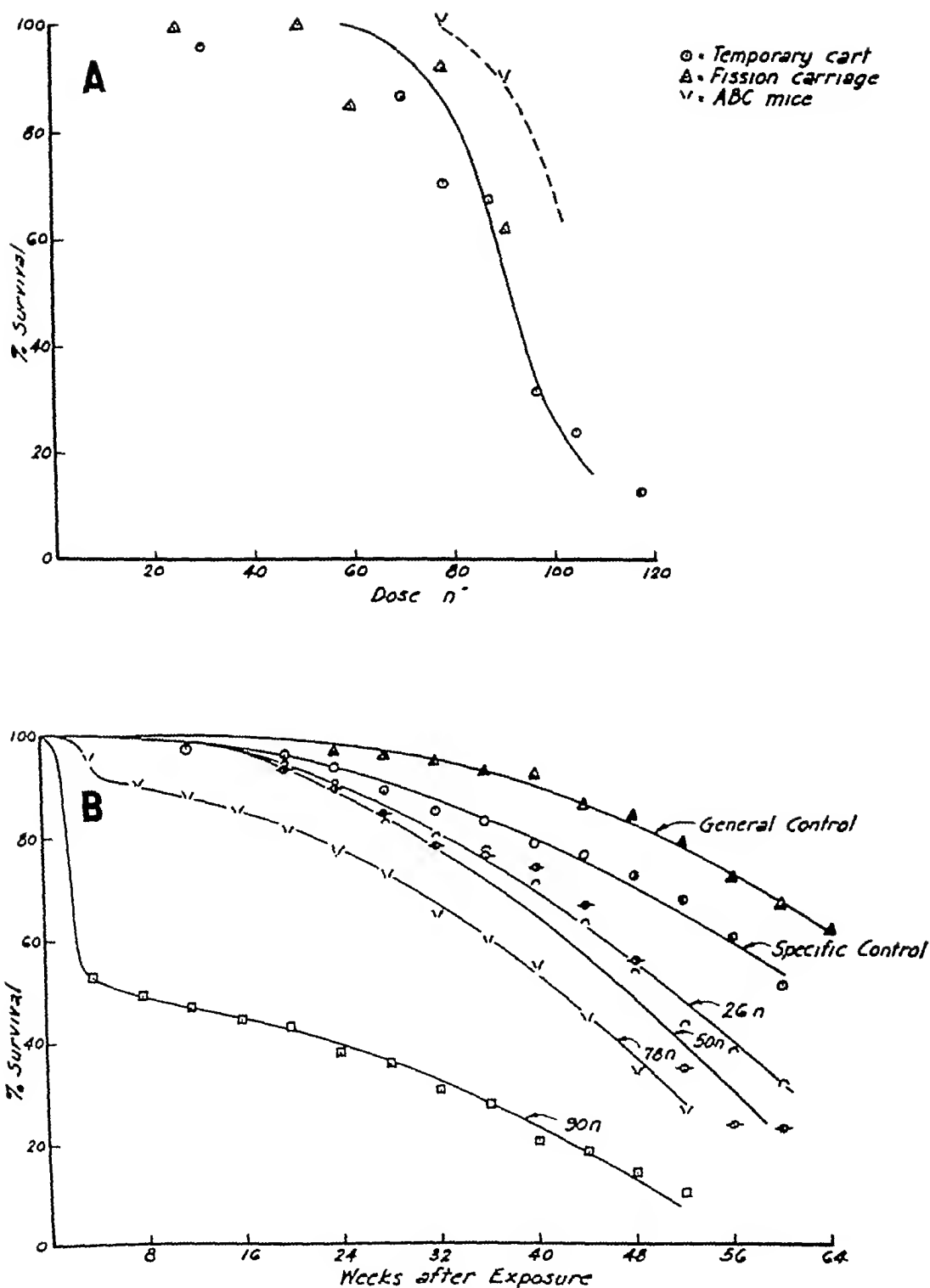


Fig 4 A Curves showing percentage of CF_1 mice surviving three weeks as a function of dose, in n , of fast neutrons (circle points obtained with one kind of exposure chart and triangle points with another). The two ∇ points (broken line curve) were obtained with ABC mice. B Curves showing percentage survival as a function of time for controls and animals receiving different amounts of fast neutrons

with respect to sex, although the CF_1 males were found to be less reliable as test material because of pugnacious instincts. Some differences were noted with respect to species. The ABC mice were definitely more resistant than CF_1 , more exposure was required to produce the same degree of shortening of life.

Terminal changes were mainly of two types: generalized atrophy (premature aging) and mediastinal lymphomatosis. The incidence of lymphoma was about 15 per cent in controls and was raised to two or three times that figure by the 115

dose is approximately 92 n. From the limited data the ABC mice appear to be more resistant.

Ninety-two n as the lethal dose for 50 per cent (LD_{50}) for fast neutrons is considerably less than is required to kill 50 per cent of the animals if the radiation is applied in small daily doses. If it is assumed that a three-week period is required for the lethal effects of radiation to become manifest, then that dose accumulated three weeks prior to the date when 50 per cent of the periodically exposed animals succumbed is the effective

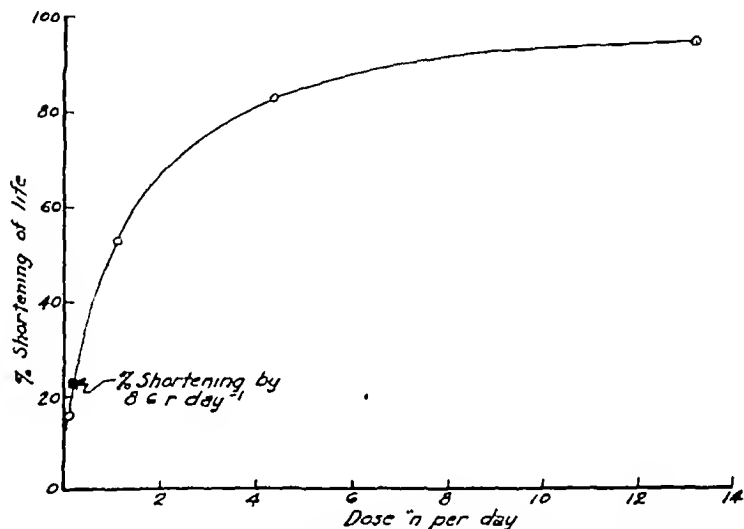


Fig 3 Curve showing percentage shortening of life in CF_1 mice as a function of daily exposure to fast neutrons

n and 86 r treatments. The incidence of ovarian growths was increased somewhat by these exposures, but it is plain that lung tumor incidence is reduced in animals that have a significantly high spontaneous incidence. Similarly, the incidence of leukemia is not enhanced by the treatments in animals with a high spontaneous incidence (C58).

Single Treatments (Fast Neutrons and Gamma Rays) Figure 4A presents a graphic summary of results obtained with single doses of fast neutrons. The results depicted show that 50 n is near the threshold for the acute lethal effects of fast neutrons, and that the 50 per cent killing

LD_{50} . In this manner, the LD_{50} for mice exposed to between 1 and 5 n per day was determined to be between 150 and 175 n. Thus, the relationships between the single dose LD_{50} and the periodic dose LD_{50} shows that an extension of a dose in time decreases its effectiveness.

The family of curves in Figure 4B shows the effects of graded doses of fast neutrons on the ability of mice to survive over a long period. The abrupt fall at the beginning of curves for 78 and 90 n are the result of some acute killing (death in three weeks) in the groups. Although the data are not too stable, there is nevertheless a definite tendency for the length of life

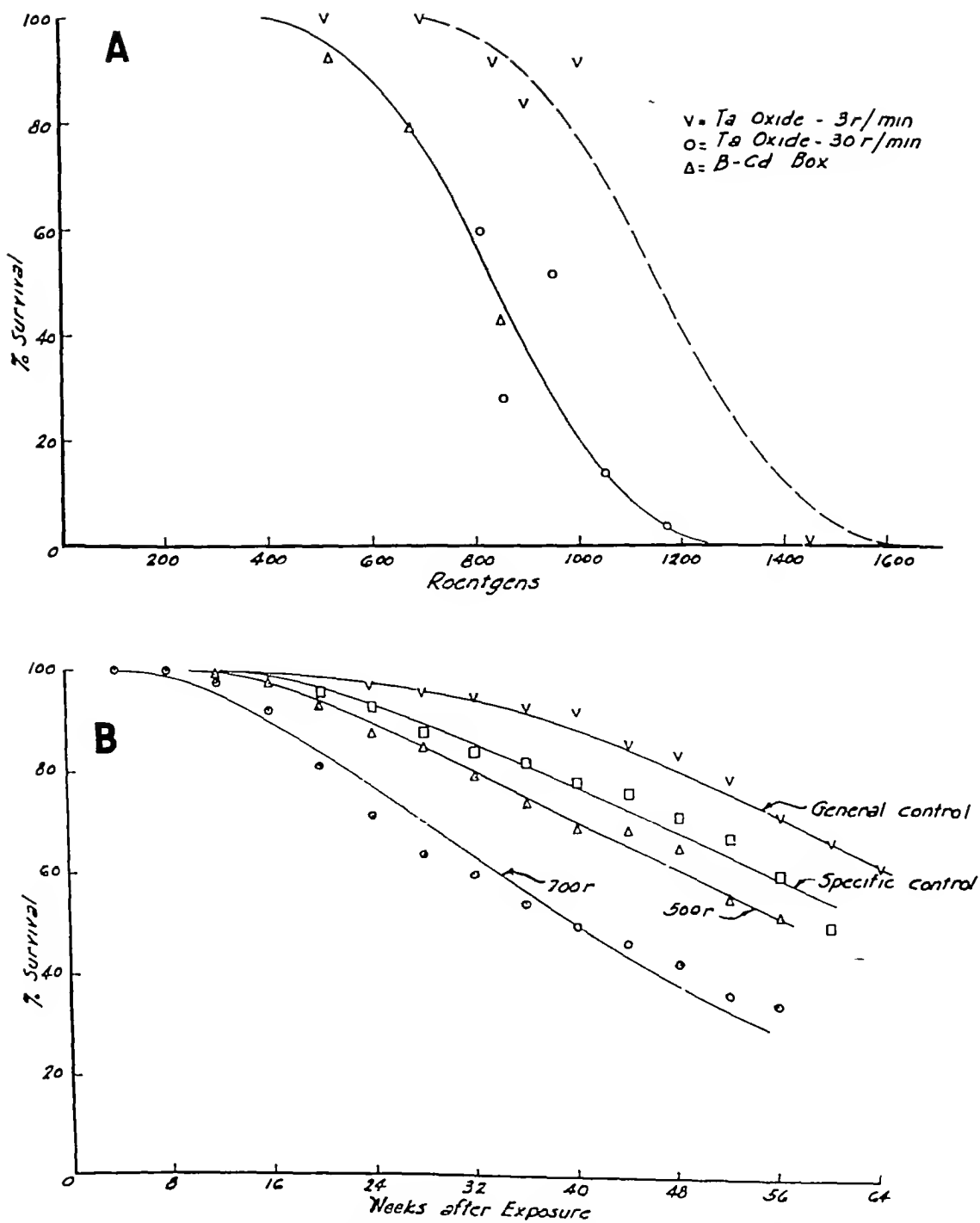


Fig 5 A Curves showing per cent of survival as a function of dose for various conditions of treatment B Per cent of survival as a function of time after single treatments with 500 to 700 r of gamma rays

to vary inversely with the size of dose administered, and the 26 n dose appears to be near the threshold range for shortening life

Figure 5 depicts the results obtained with single doses of gamma rays. The survival values in 5A are the result of one of the side issues so often encountered in pursuit of the main line of an investigation. An experiment was started to determine the effect of age on radiosensitivity. The best source of gamma rays then available had an intensity of about 30 r per minute. The results obtained with this source (triangular symbols) showed the LD50 dose to be about 840 r. Later the tantalum source was developed, with this, as used, the intensity was approximately 3 r per minute ("v" symbols). In this case the LD50 was found to be in the range of 1,100 to 1,200 r, in marked contrast with the earlier figure. The distance was then shortened for the studies with tantalum sources so that the intensity was very nearly 30 r per minute. With this arrangement, a third set of values was obtained (circular symbols). Since the values obtained with the two higher intensities are consistent with each other, it is apparent that the duration of exposure has significant effects. Analysis of the findings, in fact, showed that increasing the period of exposure ten times reduces the effectiveness for a given dose to approximately 70 per cent.

Figure 5B shows the results obtained with 500 and 700 r of gamma rays. The length of life was again found to vary with length of exposure and by comparison it was noted that the survival curve for the 700 r group reached the 50 per cent survival level at about 40 weeks, which corresponds closely to the late effects observed after a single dose of 78 n (Fig 1). From this comparison, 1 n and 9 r may be considered equally effective for producing injury roughly one year after treatment.

The ratio of biological effectiveness derived above was determined by comparing late effects of a single dose of fast neutrons with the same effects produced

by a single dose of gamma rays administered at 3 r per minute. When other criteria of effect are used or when the method of exposure is varied, different ratios of effectiveness are observed. These ratios may be summarized as in Table I.

TABLE I BIOLOGICAL EFFECTIVENESS RATIOS OBTAINED WITH FAST NEUTRONS AND GAMMA RAYS

Criterion of Effect	Type of Dose	Dose Rate Fast Neutrons	Source of Gamma Rays and Dose Rate	Biological Effectiveness Ratio (f/n)
Acute lethal	Single	3n/min	B Cd 30r/min	1.9
Acute lethal	Single	3n/min	Ta 30r/min	1.9
Acute lethal	Single	3n/min	Ta 3r/min	1.12
Delayed lethal	Single	3n/min	Ta 3r/min	1.9
Delayed lethal	Periodic	3n/min	Ta 3r/min	1.35

With the exception of the last ratio listed in Table I, all the ratios seem to be of the same general order of magnitude, as had been found with single doses of x-rays and cyclotron neutrons, that is, 1 n to 7.5 r. Only the last ratio noted in the table would appear to be of a different order of magnitude. This last figure may be changed when final and more accurate results can be determined, but it is felt that it will continue to be significantly different from the rest.

Terminal autopsies were performed on all single dose animals as for those receiving periodic doses, and essentially the same kind of changes were seen—generalized atrophy and mediastinal lymphomatosis. In the case of the animals treated with 500 and 700 r of gamma rays, the lymphoma incidence reached levels above 60 per cent, appreciably higher than obtained with any other type of treatment (cf Tables II and III).

Hematological changes in animals treated with single doses were negative except for the acute reaction—a leukocyte decline during the first four to seven days and a recovery during the second and third weeks. Only slight, if any, evidence

of weight, some increase of tumor incidence in organs other than hemopoietic, a modified blood picture, and a changed pathology and histology, all of which served as criteria of irradiation effects. It was plain that the chain of events between treatment and death did not always follow the same pathway even with identical treatments and animals of uniform type.

3 Generalized atrophy, in the case of small daily treatments, appeared to result from the inroads of sublethal damage which in time added up to the exhaustion of vital reserves. Neoplasia may or may not result directly from the atrophic condition.

4 By utilizing the various criteria of effect, different thresholds of damage were found. Survival time, which was one of the most sensitive responses, showed effects following daily exposures in the range of 0.1 n of fast neutrons and 1 r of gamma rays. In the case of single exposures, threshold levels were not determined.

5 Threshold responses of the peripheral blood were at least a factor often less sensitive than threshold survival responses in CF₁ mice.

6 Some differences were noted in the responses of different strains of animals, but these were more a matter of degree than of type, and in some instances could be associated with species characteristics.

7 No fundamental differences were observed in the responses of the different sexes, although the effects being studied were sometimes obscured by sex features, such as pugnaciousness in CF₁ males.

8 The r/n ratio of gamma rays to fast neutrons for the different effects varied roughly from 8 to 1 to 35 to 1 for the conditions and methods used.

9 The degree of acute damage (as measured by survival after single massive

dose exposures) varies not only with dose but also with the intensity of irradiation, a ten-fold increase in exposure time for gamma ray treatments reduced the effects observed for a given dose to about 70 per cent.

10 The accumulative evidence indicates that the degree of biologic effect varies not only with dose but also with density of ionization produced.

11 The incidence of lymphoma following exposure to penetrating radiations was raised from 15 per cent in the controls to well over 60 per cent in groups receiving single doses of 500 and 700 r of gamma rays.

12 Lung tumor incidence was increased little, if any, by the treatments given. This was true of CF₁ and A mice, both of which have a high spontaneous lung tumor incidence and a demonstrated ability to respond to other carcinogenic agents. Because of the trace of positive evidence, because of the external sources of radiation used, and because the animals used were short-lived compared with human beings, the question of radiation carcinogenesis in the lungs cannot be fully dismissed.

13 When sublethal doses of beta rays are applied to rats and mice (particularly Sprague-Dawley rats) abnormalities are produced in the skin, especially of the malignant types. Following doses of 4,000 to 5,000 rep, animals that ordinarily have no skin lesions all showed skin carcinomas, including nearly every type, some animals having 50 to 100 loci.

14 It is significant that hemopoietic-tissue tumors were obtained with penetrating radiation and skin tumors with surface-absorbed radiations.

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TABLE II TUMOR INCIDENCE FOLLOWING A SINGLE DOSE OF FAST NEUTRONS

Dose	Eligibles	Lymphoma	Ovarian Tumors	Lung Tumors
90 n	45	13 (27%)	16 (36%)	16 (36%)
78 n	63	19 (30%)	23 (37%)	24 (38%)
50 n	75	24 (32%)	30 (40%)	27 (36%)
26 n	76	17 (22%)	27 (36%)	37 (49%)
0 n	108	15 (14%)	18 (17%)	57 (53%)

of injury to the peripheral blood picture could be seen at three weeks

Slow Neutron Effects The terminal effects and early death obtained with slow neutrons resembled in every respect those obtained with fast neutrons and gamma rays. This was also true so far as the effects on the peripheral blood picture was concerned. The studies have

TABLE III TUMOR INCIDENCE FOLLOWING A SINGLE DOSE OF GAMMA RAYS

Dose	Eligibles	Leukemia	Ovarian Tumors	Lung Tumors
700 r	66	42 (64%)	16 (24%)	13 (20%)
500 r	45	30 (67%)	12 (27%)	15 (33%)
0 r	108	15 (14%)	18 (17%)	57 (53%)

not yet advanced far enough, however, to permit a satisfactory quantitative comparison of the slow neutron doses with those of fast neutrons and gamma rays required to produce a given effect.

Beta Ray Effects Rather extensive studies with beta rays have been carried out by Raper, and his results are available in various project reports. Reference will be made here only to the late effects. When beta rays from P^{32} are used, the energy absorption is limited almost completely to the skin, in contrast to the generally uniform distribution obtained with the other radiations. The lethal dose in case of beta rays varies with the size of the animal, being in the range of 4,500 rep for CF_1 mice and 7,000 for Sprague-Dawley rats. Animals which survive sublethal doses show an acute reaction consisting of some epilation, suppuration of the skin with some open lesions, a sloughing of the main distal portions of the ears, and irritation of the eyes with

consequent blindness. Recovery takes place over a period of weeks, and a fairly stable state is eventually reached.

In animals of the type just described, and more particularly those showing a less severe reaction, malignant skin lesions and other abnormalities begin to appear at six to ten months after the single treatment. The tumor forms vary from small papillomas to the most malignant carcinomas and include practically every type of skin reaction known in tumor pathology.

Developmental abnormalities in the form of changes in color, texture, and type of hair, duplication of claws, horn-like extensions from the nose or eye, and deformed appendages were frequent in Sprague-Dawley rats receiving single doses of 4,000–5,000 rep. The incidence of skin tumors in such animals is 100 per cent and the number of loci of tumors arising may reach 50 to 100. The reactions in CF_1 mice are of the same type, but occur less frequently. Small daily treatments have not as yet given significant skin responses, but a sufficient range of doses has not been tried.

It is significant that the malignant response elicited by penetrating radiations, irrespective of type, consisted of hemopoietic tissue tumors, whereas that elicited by non-penetrating radiations was limited to the skin.

GENERAL SUMMARY

1 Experiments have been carried out with CF_1 , ABC, A, and C58 mice to determine the late effects of periodic and single exposures of fast neutrons, slow neutrons, and gamma rays (penetrating radiations). Similar experiments were carried out with beta rays, the absorption of which was limited almost exclusively to the skin.

2 In general the late effects resulting from exposure to penetrating radiations, irrespective of the method of exposure, consisted of generalized atrophy and neoplasia of hemopoietic organs. Both effects were attended by shortened life span, loss

of weight, some increase of tumor incidence in organs other than hemopoietic, a modified blood picture, and a changed pathology and histology, all of which served as criteria of irradiation effects. It was plain that the chain of events between treatment and death did not always follow the same pathway even with identical treatments and animals of uniform type.

3 Generalized atrophy, in the case of small daily treatments, appeared to result from the inroads of sublethal damage which in time added up to the exhaustion of vital reserves. Neoplasia may or may not result directly from the atrophic condition.

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(See page 360 for Spanish Summary)

SUMARIO

Efectos Biológicos de la Irradiación con Pilas

En un reactor de pilas varias radiaciones de alta energía (neutrones veloces y lentos, rayos gamma, rayos beta, etc) se asocian a la reacción vinculada con la cadena del uranio. Es sabido que todas esas radiaciones ocasionan efectos biológicos nocivos, por lo cual constituyen riesgos para la salud.

Tratando de comprender mejor la naturaleza de las lesiones evocadas y de obtener al mismo tiempo datos relativos a las dosis límites y de tolerancia, se llevaron a cabo numerosos experimentos en animales, usando principalmente para las pruebas cuatro razas de ratones (CF₁, ABC, A, C58) y una raza de ratas (Sprague-Dawley). Las diversas radiaciones fueron obtenidas por medio de filtración selectiva, emisores secundarios e isotopos radioactivos. Los tratamientos fueron administrados en forma de dosis masivas únicas y de dosis pequeñas diarias. Los rayos usados, con excepción de los beta, fueron penetrantes, y en su mayor parte se distribuyeron por todo el cuerpo de los animales.

El resultado reveló que la duración de la vida variaba en razón inversa a la cantidad de exposición, y además que el efecto variaba en razón directa a la concentración de yones en espacio y tiempo.

El efecto terminal producido al usar rayos penetrantes tomó principalmente dos formas: atrofia generalizada y neoplasia de los órganos hematopoyéticos. La atrofia se acompañó de leucopenia, emaciación, pérdida de peso y muerte prematura. Las neoplasias observadas consistieron principalmente en linfomatosis mediastínicas, elevándose la frecuencia de éstas, de menos de 15 por ciento en los testigos a más de 60 por ciento en algunos de los grupos de experimentación.

Cuando se usaron rayos no penetrantes las alteraciones se limitaron principalmente a la piel. Varios meses después de administrar dosis masivas únicas había presentes anomalías cutáneas de todo género, y en animales que rara vez muestran patología cutánea, la incidencia del carcinoma se había elevado a 100 por ciento y las localizaciones por animal subían hasta 50 a 100.

La relativa efectividad de los neutrones veloces, comparados con los rayos gamma, pareció ser netamente mayor al tomar en cuenta las modificaciones tardías más bien que las agudas. En lo tocante a acortamiento de la vida, el nivel límite de exposición diaria quedó en la escala de 1 r de rayos gamma y algo por debajo de 0.1 n.



Carcinogenic Properties of Radioactive Fission Products and of Plutonium¹

HERMANN LISCO, M D, MIRIAM P FINKEL, Ph D, and AUSTIN M BRUES, M D

Chicago, Ill.

A SERIES OF STUDIES dealing with the late effects of internal and external irradiation upon experimental animals were undertaken by the Biology Division of the Clinton Laboratories at Oak Ridge and by the Biology Division of the Metallurgical Laboratory, University of Chicago. The results of the studies concerned with external gamma and beta rays and neutrons have been discussed by Dr P S Henshaw and Dr J R Raper. In the experiments at Chicago a number of representative radioactive isotopes were chosen for study, isotopes which are released in the fission of uranium. One of the end products of the fission process is plutonium (Pu^{239}), and particular attention was paid to this substance. At the time these chronic experiments were undertaken, a limited amount of information was available concerning acutely toxic levels and distribution of plutonium.

An intelligent appreciation and evaluation of health hazards, whether by ingestion or inhalation or by way of wound contamination with minimal amounts of radioactive substances while working in potentially contaminated laboratories, is, of course, difficult without experimentation. It was with this in mind that the following experiments were undertaken, even though it was realized that it is notoriously difficult to design animal experiments which precisely duplicate the human hazards.

The late effects of various modes of treatment with Sr^{90} , ^{90}Y , Ce^{144} , Ra, and Pu^{239} were studied in mice, rats, and rabbits. Sr^{90} , ^{90}Y , and Ce^{144} are pure beta emitters with energies of 1.5, 1.5, and 0.35

Mev, respectively, and half lives of 55, 57, and 275 days, respectively. Plutonium is an alpha emitter with a half life of about 25,000 years.

Radiostrontium, like radium, was largely concentrated in bone, and the average total retention at fourteen days was 45 per cent for the mouse, 59 per cent for the rat, and 21 per cent for the rabbit, these figures are corrected for decay. Almost all of the retained Sr^{90} was found in the skeleton, and consequently bone tumors were readily produced. The incidence of bone tumors was approximately proportional to the dose administered, and the latent period—in no case less than about 200 days—increased gradually with decreasing dose. In the animal species studied, single and multiple bone tumors were observed, and in many individuals widespread metastases occurred, especially in rats and rabbits. Bone tumors were produced in considerable numbers by doses ranging from 50 to 0.05 microcuries per gram, both with single and with monthly repeated injections. Osteogenic sarcoma induced by Sr^{90} involved the long bones in preference to the spine, a fact which will be discussed briefly later.

It is not clear as yet whether Sr^{90} had any effect on the incidence of spontaneous lymphoma in mice.

Radio-yttrium and cerium, after either intravenous or subcutaneous administration, also produced sarcomas in the skeletal system. These tumors localized primarily in the long bones.

When plutonium and yttrium (YPO_4) were given subcutaneously or intramuscularly to mice, various manifestations of radiation damage were observed locally

¹ The work reported herein was done in the Metallurgical Laboratory of the University of Chicago and the Biology Division of the Argonne National Laboratory, Chicago under the Manhattan Project. This paper is a brief version of material to be published in the Plutonium Project Record of the Manhattan Project Technical Series. Presented at the Thirty-Second Annual Meeting of the Radiological Society of North America, Chicago, Ill. Dec. 1-6, 1946.

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SUMARIO

Propiedades Carcinogenas de los Productos Radioactivos de Fisión y del Plutonio

Los efectos tardíos de ciertos isótopos radioactivos liberados en la fisión del uranio fueron estudiados en animales de experimentación. Al cabo de un período mínimo de 200 días de latencia después de la inyección de radioestroncio (Sr^{90}) a dosis de 5.0 a 0.05 microcuries por gramo, se presentaron osteomas, principalmente en los huesos largos. Produjéronse tumores semejantes con radio-itrinio (Y^{91}) y cerio (Ce^{144}). La administración subcutánea e intramuscular de plutonio (Pu^{239}) y de itrinio (YPO_4) fué seguida de alteraciones

locales, incluso formación de fibrosarcomas malignos. Las inyecciones de plutonio a dosis de 4.5 a 0.05 microgramos por gramo produjeron osteomas, pero en contraposición a los debidos a los otros isótopos, donde predominaron fué en el raquis. Observáronse lesiones hepáticas en los animales que recibieron plutonio, cerio y fosfato de itrinio, pero no se descubrieron hepatomas. En las ratas alimentadas con itrinio (Y^{91}) aparecieron carcinomas del colon.

These included graying of hair, epilation, ulceration of the skin, and destruction and atrophy of muscles, often followed by spontaneous amputation of the injected leg. Of particular interest has been the occurrence locally of malignant fibrosarcomas in a very high percentage of animals at doses ranging from 0.5 to 0.05 μgm per gram of Pu^{239} and at doses of 1.5 to 0.05 μc per gm of YPO_4 . In other words, a total of 1 μgm of plutonium or 1 μc of YPO_4 injected locally under the skin induced fibrosarcomas even though a certain portion of the injected dose was removed from the site of injection and was distributed throughout the body and partially excreted.

Bone tumors were seen frequently in mice, rats, and rabbits injected with plutonium at levels ranging from 4.5 to 0.05 μgm per gram. The minimal latent period again was about 200 days. The majority of the plutonium-induced tumors occurred in the spine, often producing hind leg paralysis and urinary retention as the first clinical symptoms. An explanation for this difference in localization probably lies in the fact that plutonium has a greater affinity for collagenous tissue than for bone proper. This fact has been clearly demonstrated by radioautographs.

The distribution of bone tumors in the skeleton of rats and mice with various radioactive isotopes is summarized in Table I.

TABLE I DISTRIBUTION OF BONE TUMORS (PER CENT)

Agent	Spine	Long Bones	Pelvic Bone	Jaw	Ribs
Pu	62	8	15	7.5	7.5
Sr	22	61	6	10	1
Y	14	86	0	0	0
Ce	16	74	5	0	5

Both plutonium and cerium showed a consistently high concentration in the liver. Hence, liver damage was frequently noted in animals at the higher dose levels, but no true liver tumors have been seen to date. Small adenomata have, however, occurred in the liver in the process of regeneration

and repair. The liver damage produced was unique, as it probably represented direct radiation damage of this organ, which is not very vulnerable to high doses of external irradiation. A third compound which also produced liver damage upon intravenous injection was the insoluble salt, yttrium phosphate. An interesting corollary to these experimental studies is the fact that "thorotrast" (a colloidal suspension of thorium dioxide) is frequently used in human diagnostic work. It behaves not unlike the aforementioned substances in its distribution in the human and animal body. Therefore, it may be well to keep this in mind, particularly in diagnosis of those patients who do not suffer from an incurable disease.

Another example of the carcinogenic properties of internal irradiation was the occurrence of carcinoma of the colon in rats which had been fed Y^{91} . This substance was practically not absorbed from the intestine and, when fed by stomach tube, remained longest in the colon. One group of rats received a single feeding of from 1.0 to 6.0 millicuries. Of a total of 33 animals, 4 died with adenocarcinoma of the colon. The earliest tumor was seen 135 and the last 506 days after feeding. A second group of animals was given repeated feedings of 0.46, 0.20, or 0.06 millicuries of Y^{91} per feeding over a period of three months, so that the total accumulated doses were 31.20, 15.60, and 4.68 millicuries, respectively. Clinically all animals appeared well during the feeding period and growth was not impaired. Six of the 8 animals at the two higher dose levels died with carcinoma of the colon between 304 and 548 days after the first feeding. No malignant lesions were observed at the lowest level.

It would not have been possible to carry out these experiments without the help of many people too numerous to mention here. Their enthusiastic cooperation in these studies is gratefully acknowledged.

ily stated, and few, if any, fundamental facts had emerged. When large numbers of the leading scientific and industrial workers of the country were subjected to the risks of exposure and the probability of mass exposure of the Armed Forces and civilians became great, the need for such fundamental knowledge became very acute. While it was recognized that the real solution to the problems of prevention, detection, and treatment would come from an understanding of the basic mechanism or mechanisms by which radiations affect biological systems, a more direct approach was needed and taken.

While the effects on man of, and the tolerance to, α - and gamma-radiations were known to some extent, such knowledge was almost completely lacking regarding neutrons and beta rays, especially when the total body exposure had to be considered. No maximum permissible exposure (tolerance dose) had ever been established for such rays.

A comparatively new hazard was created by the process of making plutonium. Many new radioactive elements were being produced in very large quantities. The radium industry, and in particular the radium dial painting part of it, had demonstrated the hazard of radium and its decay products becoming deposited in the body. Where these new radioactive elements—some of which were gases, others volatile materials, and all others capable of being dust—would go in the body and what they would do there was unknown.

In view of the above, there should no longer be any doubt as to why extensive medical and biological research was undertaken as a part of the Plutonium Project. The Metallurgical Laboratory in Chicago with its laboratory studies, the Clinton Laboratories in Oak Ridge with their pilot plant activities, and the Dupont Plant at

Richland with its production activities were the main centers of the medical and biological research. The Radiation Laboratory at the University of California, having pioneered in the field of the biological study of radioactive elements, was obviously the place where the metabolic study of such elements could proceed rapidly. The National Cancer Institute of the Public Health Service, having already initiated studies of the effects of small daily doses of α - and gamma-rays on laboratory animals, was the obvious place to investigate the problem of tolerance to radiation. Memorial Hospital of New York with its Heublein Unit and the University of California Hospital with its million-volt unit were logical places to extend the studies relative to the effects of total body irradiation on the blood. Other problems, such as the physical measurement of the radiations and the chemical toxicity of uranium and other elements, were also investigated, but do not form a part of this symposium.

It must be mentioned here that under the Manhattan Project were many other units than the Plutonium Project. Some of these, such as the University of Rochester and Columbia University, were investigating similar and related medical and biological problems. Their activities are not discussed here, since they were not part of the Plutonium Project.

The medical, biological, and physical sections had scientists from all parts of the country helping in the work. To name them would require almost as much space as this editorial. They have the satisfaction of knowing that they took part in a great enterprise. A few are getting some scientific recognition by the publications in this issue of *RADIOLOGY*. It is to be hoped that the work and names of all will soon be known through other such publications.

ROBERT S. STONE, M.D.

EDITORIAL

The Plutonium Project

The Plutonium Project was that part of the organization for the production of atomic bombs charged with the scientific task of finding out how to make and isolate plutonium and with the industrial task of producing purified plutonium in sufficient quantities to be useful. It was organized and operated in the beginning under the Office of Scientific Research and Development. It went forward to a successful conclusion with the Manhattan District of the U S Engineers acting as the co-ordinating, expediting, and financing agency. The scientific work was performed under a contract with the University of Chicago and the industrial development with the E I du Pont de Nemours Company. Scientists, industrial engineers, and others of many skills were brought to Chicago to work in the Metallurgical Laboratory of the University of Chicago, as it was called during the war.

One might well ask why the biological work on which a symposium presented at the meeting of the Radiological Society of North America and the papers in this issue of RADIOLOGY are based was done in connection with such a project. The answer is obvious to all who know even superficially how plutonium was produced. Uranium fission, chain-reacting piles, fission products, and artificial radioactive materials are now household words. They were all a part of the "Plutonium Project."

To make plutonium, it was necessary to utilize the great numbers of neutrons produced during the fission of U^{235} to transmute U^{238} into neptunium. This element then changed to plutonium by radioactive decay. The process produced recoil nuclei, alpha rays, beta rays, fast neutrons, slow neutrons, and gamma rays in intensi-

ties never before dreamed probable or possible. Moreover, the plutonium when formed was embedded in uranium along with fission products whose radioactivity was equivalent to thousands of grams of radium. The workers in the laboratories and plants had to be protected and the health of the public in surrounding territories had to be safeguarded.

The problem of the maximum permissible exposure (tolerance dose) that would produce no immediate or late changes was no longer of interest only to a limited group of radiologists and radium workers, but became one of significance to thousands of people. The scientific data on which it was based were found to be very sketchy. What are the first changes produced by exposures just above the tolerance level? Is the peripheral blood picture as reliable an indicator of over-exposure as radiologists have considered it to be? Are there any other changes produced that can be detected by known or newly developed clinical tests? Can a person ever recover completely and entirely from any dose of radiation big enough to produce detectable effects? Are there any methods of treatment that will aid in recovery? How much radiation is necessary to kill a man? These and many other problems became real and acute when feet of concrete instead of millimeters of lead must be used to protect and when accidental or intentional exposure of the whole body became a real possibility.

A considerable literature existed on the physiological and histological changes that occur following exposure to ionizing radiations, but the experimental material was usually too limited, the data given by one worker were not comparable with those of others, the doses were often unsatisfactor-

ily stated, and few, if any, fundamental facts had emerged. When large numbers of the leading scientific and industrial workers of the country were subjected to the risks of exposure and the probability of mass exposure of the Armed Forces and civilians became great, the need for such fundamental knowledge became very acute. While it was recognized that the real solution to the problems of prevention, detection, and treatment would come from an understanding of the basic mechanism or mechanisms by which radiations affect biological systems, a more direct approach was needed and taken.

While the effects on man of, and the tolerance to, x- and gamma-radiations were known to some extent, such knowledge was almost completely lacking regarding neutrons and beta rays, especially when the total body exposure had to be considered. No maximum permissible exposure (tolerance dose) had ever been established for such rays.

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ROBERT S. STONE, M.D.

REFRESHER COURSES POST-GRADUATE INSTRUCTION

A series of Refresher Courses will be presented at the time of the Thirty-Third Annual Meeting of the Radiological Society of North America, at the Statler Hotel, Boston, Mass., Nov. 30 through Dec. 5, 1947.

These courses of post graduate instruction will be given from 2 to 5 P.M. and 7 to 9 P.M. on Sunday, Nov. 30, and from 8:30 to 10 A.M. daily thereafter during the meeting. No other meetings will be scheduled for these hours, and the courses have been so arranged that those interested in a particular subject may enroll in a related series as far as possible.

Admission will be by ticket only, and reservations will be made in the order in which applications are received. Non members will be charged \$2.00 for each course, up to a maximum of \$5.00 for the entire

series. Reserve officers still on active duty, residents and fellows in radiology will be exempt from these charges.

Read the description of the courses, noting particularly the days upon which they are offered, study the Plan of Presentation and select carefully your choice for each day, as the number attending each course will be limited. If the directions listed on the Plan of Presentation and Instructions for Enrollment are observed, errors will be avoided.

If the Refresher Courses are not filled by the time of the meeting, tickets will be available at the registration desk, Sunday, Nov. 30, and thereafter.

It may be necessary to alter or revise some of the courses and to change some of the instructors. We shall, however, adhere as closely as possible to the choices made.

Course No. 1 Sunday, 2-5 P.M.

Roentgenologic Manifestations of Acute Abdominal Diseases

LEO G. RIGLER, M.D.

University of Minnesota
Minneapolis, Minn.

1. Roentgen technic in acute abdominal disorders. Special technical procedures are necessary in the handling of patients. Variations from the usual technic in the examination of the abdomen, the difficulties, and special procedures necessary will be detailed.

2. Indications for roentgen examination in the acute abdominal disorders. The various acute processes in the abdomen in which roentgen examination is of great assistance in establishing either the diagnosis or aiding in determining the extent and nature of the process will be presented.

3. Analysis of the scout film of the abdomen.
(a) The normal appearance of the roentgenogram of the abdomen without contrast medium. The soft tissue shadows, the appearance of the gastrointestinal tract with and without preparation and under varying conditions will be demonstrated.

(b) The abnormal roentgenogram without contrast medium. A discussion of the physiologic and pathologic factors in the production of changes in the abdomen will be undertaken. An analysis of the various findings which may be obtained with different types of acute abdominal disorders and their differential diagnosis will be presented.

Demonstrations will be given of the findings in

- (1) Peritonitis
- (2) Intra abdominal abscess
- (3) Small intestinal obstruction
- (4) Large intestinal obstruction

4. Value of x-ray examination in the acute abdominal disorders. The reliability of the various x-ray signs and their contribution toward the practical handling of the patient will be discussed.

Course No. 2 Sunday, 2-5 P.M.

Diagnosis, Treatment, and Prognosis of Carcinoma of the Cervix and Endometrium

J. A. DEL REGATO, M.D.

Columbia, Mo.

The course will review the important questions of diagnosis, including technic of examination and clinical staging, of carcinoma of the cervix. This will be followed by a discussion of external pelvic roentgen therapy and the different technics of intracavitary curie therapy as well as transvaginal roentgen therapy. There will also be a discussion of the indications for surgery and radiotherapy and an analysis of the results of the different methods of treatment of carcinoma of the uterus.

Course No. 3 Sunday, 7-9 P.M.

Film Reading Session

MERRILL C. SOSMAN, M.D.

Peter Bent Brigham Hospital, Boston, Mass.

Presiding

JOHN D. CAMP, M.D., Mayo Clinic
L. HENRY GARLAND, M.D., San Francisco, Calif.
FRED J. HODGES, M.D., University of Michigan
LEO G. RIGLER, M.D., University of Minnesota

This is an opportunity for the members to present their interesting cases, but, in order to make this session of real teaching value, it has been decided that all cases must be approved by Dr. Sosman in

advance and must fulfill certain requirements, namely,

- (1) That they be proved beyond a reasonable doubt
- (2) That it be possible to make the correct diagnosis either from the x-rays, history, physical examination, laboratory findings, or any combination of these
- (3) That they be of interest and of teaching value

Anyone desiring to present cases should write directly to Merrill C. Sosman, M.D., Peter Bent Brigham Hospital, Boston, Mass., outlining the case and the proof. If the case is accepted, the one presenting it will be asked to make lantern slides (standard, $3\frac{1}{4} \times 4\frac{1}{4}$ inch size) and to bring the original x-rays for the "experts." No cases can be considered that are submitted later than Nov. 1.

Course No 4 Sunday, 7-9 P.M.

Therapy Information

R. R. NEWELL, M.D.

Stanford University, San Francisco, Calif.

Presiding

MILTON FRIEDMAN, M.D., New York, N.Y.
 LOWELL S. GOIN, M.D., Los Angeles, Calif.
 B. V. A. LOW BEER, M.D., Los Angeles, Calif.
 EDITH H. QUIMBY, Sc.D., New York, N.Y.

You are invited to present cases of particular interest or problems in radiation therapy to the professors, and to stump them if you can.

Dr. Newell invites all of those who are interested in radiation therapy to present their cases to him by mail at 50 Yerba Buena Ave., San Francisco 16, Calif., in advance of the session.

In addition to the questions and answers from the members, the panel will present discussions of the various phases of radiation therapy, including contraindications to irradiation and choice of type of radiation therapy for various lesions.

Course No 5 Monday, 8 30-10 A.M.

When, Why, and How Should Contact Therapy be Used?

LOWELL S. GOIN, M.D.

Los Angeles, Calif.

- 1 Historical
- 2 Apparatus employed (actual machine and tube in operation)
- 3 Physics involved
- 4 Limitations of method
- 5 Fields of application
 - (a) External
 - (b) Intracavitary
 - (c) Surgical

6 Technique and dosages employed

7 Results evaluated

Course No 6 Monday, 8 30-10 A.M.

(This course will be repeated on Tuesday, 8 30-10 A.M.)

The Radiologic Aspects of Urinary Tract Disease

FRED J. HODGES, M.D.

University Hospital
 Ann Arbor, Mich.

X-ray methods employed in the field of urology will be reviewed. The pathological situations which can be detected by such procedures will be summarized and illustrated. Desirable relationships between urologist and radiologist will be discussed.

Course No 7 Monday, 8 30-10 A.M.

Roentgenological Classification of the Pneumonias with Special Reference to the Structures Involved

L. R. SANTE, M.D.

St. Louis, Mo.

In recent years many causes have been found for pneumonia other than the pneumococcus. Many of these pneumonias have been described as atypical pneumonias of unknown etiology. The etiologic agents for these unusual forms are so multiple and varied that they may cause confusion to the radiologist. To clarify the situation, a comparative study of the roentgen manifestations of the various types of pneumonia with the pathological pictures which they produce has been undertaken.

Course No 8 Monday, 8 30-10 A.M.

Roentgenography of the Skull

JOHN D. CAMP, M.D.

Section on Roentgenology, Mayo Clinic
 Rochester, Minn.

This is a discussion of the roentgenographic changes associated with lesions of the skull, of local and systemic origin. The changes associated with intracranial disease also will be considered.

Course No 9 Monday, 8 30-10 A.M.

Classification, Diagnosis, and Treatment of Cancer of the Skin

BERNARD P. WIDMANN, M.D.

Philadelphia, Penna.

Discussion of diagnosis, classification, how and why cancer of the skin should be treated, including treatment of hemangiomas.

Plan of Presentation

SUNDAY, Nov 30 2-5 P M	MONDAY, Dec 1 8 30-10 A.M	TUESDAY, Dec 2 8 30-10 A.M
1 Roentgenologic Manifestations of Acute Abdominal Diseases Leo G Rigler M D	5 When, Where, and How Should Contact Therapy Be Used? Lowell S Goin, M D	10 Roentgenology of the Stomach and Duodenum Robert P Ball, M D
2. Diagnosis, Treatment, and Prognosis of Carcinoma of the Cervix and Endometrium Juan A del Regato, M.D	6 The Radiologic Aspects of Urinary Tract Disease (Repeated Tuesday) Fred J Hodges, M D	11 The Radiologic Aspects of Urinary Tract Disease (Repetition of course No 6) Fred J Hodges, M.D
J	7 Roentgenological Classification of the Pneumonias with Special Reference to the Structures Involved L. R Sante, M D	12 Roentgenological Findings and Differential Diagnosis of Skeletal Diseases (Continued Wednesday) Paul C Hodges M D
7-9 P M	8 Roentgenography of the Skull John D Camp M D	13 Encephalography and Ventriculography John D Camp M.D
3 Film Reading Session Merrill C Sosman, M D L Henry Garland M D Leo G Rigler, M.D John D Camp, M D Fred J Hodges M D	9 Classification, Diagnosis, and Treatment of Cancer of the Skin Bernard P Widmann, M.D	14 Dosage Problems in the Use of Radioactive Isotopes G Failla Ph D
4 Therapy Information R. R Newell M D Milton Friedman, M D Lowell S Goin, M.D B V A Low Beer, M.D Edith H Quimby, Sc D		

Plan of Presentation

WEDNESDAY, Dec 3 8 30-10 A M	THURSDAY, Dec 4 8 30-10 A M	FRIDAY, Dec 5 8 30-10 A M
15 Roentgenologic Findings in the Small Intestine Robert P Ball, M D	20 Roentgenologic Diagnosis of Diseases of the Colon David G Pugh, M D	25 Diseases of the Gallbladder with Remarks on Cholangiography and Pertinent Pancreatic Disorders Wendell G Scott, M D
16 Clinical Pathological Significance and Differential Diagnosis of Segmental Collapse of the Lungs Laurence L Robbins, M D	21 (1) The Roentgen Changes in Primary Tuberculosis (2) Roentgen Examination of the Thymus John Caffey, M D	26 Congenital Obstructive Lesions of the Alimentary Tract John Caffey, M D
17 Roentgenological Findings and Differential Diagnosis of Skeletal Diseases (<i>Continued from Tuesday</i>) Paul C Hodges M D	22 The Treatment of Carcinoma of the Breast by Radiation Theodore P Eberhard, M D	27 Classification, Diagnosis, and Treatment of Benign Lesions of the Female Genital Tract James A Corscaden, M.D
18 Practical Problems in Radium Dosage Measurements Edith H Quimby, Sc D	23 Practical Problems in X ray Dosage Measurements J L Weatherwax, M S	28 Diagnosis and Treatment of the Lymphoid Tumors Hugh F Hare, M D
19 When, Why, and How Should Transvaginal Irradiation Be Given? Arthur W Erskine, M D	24 Radiotherapy of Cancer of the Pharynx and Larynx (<i>Continued Friday</i>) Maurice Lenz, M D	29 Radiotherapy of Cancer of the Pharynx and Larynx (<i>Continued from Thursday</i>)

Course No 10 Tuesday, 8 30-10 A M
Roentgenology of the Stomach and Duodenum

ROBERT P BALL, M D

Presbyterian Hospital
 New York, N Y

This will be a discussion of the manner of examining the stomach and duodenum in routine gastrointestinal series. Both the common and rare lesions encountered will be illustrated. Comments will be made on maneuvers during fluoroscopy and projections for radiography which seem to best disclose the various lesions.

Course No 11 Tuesday, 8 30-10 A M
The Radiologic Aspects of Urinary Tract Disease

FRED J HODGES, M.D

University Hospital
 Ann Arbor, Mich

Repetition of Course No 6

Course No 12 Tuesday, 8 30-10 A M
Roentgenological Findings and Differential Diagnosis of Skeletal Diseases

PAUL C HODGES, M.D

The University of Chicago
 Chicago, Ill.

This is the first of two lectures to be given by Dr Hodges on skeletal diseases. The second one, No 17, will be on Wednesday.

At this first lecture, non ossifying osteoma, osteoid osteoma, pulmonary osteoarthropathy, pyogenic osteomyelitis, and tuberculosis will be discussed and illustrated.

Course No 13 Tuesday, 8 30-10 A M
Encephalography and Ventriculography

JOHN D CAMP, M.D

Section on Roentgenology, Mayo Clinic
 Rochester, Minn

This course will be a presentation of the fundamentals of encephalography and ventriculography and a discussion of the characteristic changes associated with the usual intracranial lesions.

Course No 14 Tuesday, 8 30-10 A M
Dosage Problems in the Use of Radioactive Isotopes

G FAILLA, Ph.D

New York, N Y

Radioactive isotopes. Availability and possible uses as tracers and for therapy.

Discussion of physical characteristics (activity, half-life, type, and energy of radiation)

Tissue dosage determinations (1) when used in "applicators," as in the case of radium or radon, (2) when introduced into the body as chemical compounds

Influence of rate of decay, elimination local concentration

Dangers in the use of radioactive isotopes internally administered

Protection of personnel

Dosage data and charts will be presented

Course No 15 Wednesday, 8 30-10 A M
Roentgenologic Findings in the Small Intestine

ROBERT P BALL, M D

Presbyterian Hospital
 New York, N Y

The roentgenographic findings in disturbances in mobility and mucosal pattern of the small intestine associated with primary and secondary nutritional deficiency states, will be illustrated and discussed. Also, the findings in some cases of intestinal tumors will be shown and comments made. The session will include remarks upon the normal anatomy and the basic principles of intestinal movement.

Course No 16 Wednesday, 8 30-10 A M
Clinical Pathological Significance and Differential Diagnosis of Segmental Collapse of the Lungs

LAURENCE L. ROBBINS, M D

Massachusetts General Hospital
 Boston, Mass

The significant factors in the roentgen diagnosis of collapse of a lung, a lobe, and the various segments thereof will be presented. Certain structures seen in the normal chest as they pertain to collapse and the major technical requirements will be brought out. It is known that accurate roentgen diagnosis depends on recognition of the fundamental process as seen on the films in addition to certain clinical observations. The important points will be emphasized.

Course No 17 Wednesday, 8 30-10 A M
Roentgenological Findings and Differential Diagnosis of Skeletal Diseases

PAUL C HODGES, M.D

The University of Chicago
 Chicago, Ill

This is the second of two lectures of which the first is scheduled for Tuesday. See Course No 12.

This second period will be devoted to arthritis with particular reference to (1) the specific

REFRESHER SERIES

THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

November 30 through December 5, 1947

HOTEL STATLER
BOSTON, MASSACHUSETTS

(Detach here)

To Register for the Refresher Courses

FILL OUT THE FOLLOWING

(Print or type)

Last Name

First Name or Initials

Street Address

City

State

CHECK THE FOLLOWING

Member R S N A ☐ Guest ☐

M D Yes ☐ No ☐

Resident or Graduate Student in Radiology ☐

Where

Reserve Officer on Active Duty ☐

Fill out, also, the enrollment diagram on the reverse side of this page

REFRESHER SERIES

INSTRUCTIONS FOR ENROLLMENT

Read the accompanying description of the courses and study the plan of presentation. It is important that you register early, the number admitted to each course will be limited by the seating capacity of the room. Reservations will be made in the order of the receipt of request, and tickets will be held for you at the Registration desk at the Hotel Statler, beginning November 30.

FEES

Members No charge

Non-Members \$2 00 for each course up to maximum of \$5 00 for entire series

Graduate students and residents in Radiology, reserve officers on active duty No charge

(Fees should accompany applications)

PLEASE INDICATE YOUR FIRST, SECOND AND THIRD CHOICES

	First Choice		Second Choice		Third Choice	
	Course No	Instructor	Course No	Instructor	Course No	Instructor
Sunday {	2-5 P M					
	7-9 P M					
Monday						
Tuesday						
Wednesday						
Thursday						
Friday						

Prior to Nov 20, 1947, send this order sheet to
C Edgar Virden, M D, Chairman, Refresher Course Committee,
320 West 47th St., Kansas City 2, Missouri

After Nov 20, 1947, mail to
C Edgar Virden, M D, c/o 'Radiological' Society of North America
Hotel Statler, Boston, Mass

(Note Your tickets will not be mailed to you but will be given to you when you register for the meeting)

arthritis, (2) osteoarthritis, (3) rheumatoid arthritis

Course No 18 Wednesday, 8 30-10 A M

Practical Problems in Radium Dosage Measurements

EDITH H. QUIMBY, Sc D, Physicist
Columbia University
New York, N Y

The development of dosage units for radium therapy will be traced briefly. Various charts and tables for determination of dosage in roentgens will be presented, and precautions regarding their use discussed. Most of the period will be devoted to working out practical problems. (An exhibit on dosage calculation will probably be presented.)

Course No 19 Wednesday, 8 30-10 A M

When, Why, and How Should Transvaginal Irradiation Be Given?

ARTHUR W. ERSKINE, M.D.
Cedar Rapids, Iowa

A discussion of various methods used to destroy the primary lesion in cancer of the uterine cervix. The advantages of, and objections to, radium therapy, contact therapy, and each of the four major modifications of the transvaginal method will be set forth in some detail. Indications, contraindications, distribution, dosage, and results will also be briefly considered.

Course No 20 Thursday, 8 30-10 A M

Roentgenologic Diagnosis of Diseases of the Colon

DAVID G. PUGH, M.D.
Mayo Clinic
Rochester, Minn.

The conduct of the examination of the large intestine will be described, and the criteria for the diagnosis of the lesions more frequently encountered there will be discussed.

Course No 21 Thursday, 8 30-10 A M

(1) Roentgen Changes in Primary Tuberculosis

(2) Roentgen Examination of the Thymus

JOHN CAFFEY, M.D.
The Presbyterian Hospital
New York, N Y

(1) Tuberculosis

Historical review of the principal contributions

Morbid anatomy of primary tuberculous complex.

Pulmonary focus

Perifocal exudate

Pulmonary atelectasis

Regional lymph nodes

Intrathoracic and extrathoracic

Localized and diffuse pleurisy

Obstructive atelectasis and emphysema

Obstructive bronchiectasis

Value of lateral and oblique projections

Differential diagnosis

Values and limitations of roentgen examinations in diagnosis and prognosis

Extrathoracic primary tuberculous complexes

(2) The Thymus

Normal anatomy and physiology

Roentgen findings

The thymus and sudden death

The thymus and "thymic symptoms"

Therapy of the thymus

Comment. Dr. John Caffey is to give two sessions on Roentgenology in Children, covering certain phases of chest and gastro-intestinal examinations wherein the findings in children differ essentially from those in adults. He will conduct this session and course No. 26, as outlined.

Course No 22 Thursday, 8 30-10 A M

The Treatment of Carcinoma of the Breast by Radiation

THEODORE P. EBERHARD, M.D.
Jefferson Medical College and Hospital
Philadelphia, Penna.

A brief discussion will be given of the various types of breast cancer, with the object of defining those types and stages of the disease considered suitable for radiation treatment, special emphasis being laid on the Haagensen-Stout criteria of operability. While it is agreed that "cure" of breast cancer by radiation is seldom, if ever, achieved, long-term arrests may be hoped for under certain circumstances and the technique followed in these cases will be described in detail. Finally, there will be time devoted to the various techniques employed in the treatment of the largest group of cases coming to the radiologist, those in which palliation of pain and relief from ulceration are the only objectives.

Course No 23 Thursday, 8 30-10 A M

Practical Problems in X-Ray Dosage Measurements

J. L. WEATHERWAX, M.S., Physicist
American Oncologic Hospital
Philadelphia, Penna.

tion, and focal-skin distance on the radiation roentgen output of an x-ray machine as measured in air

2 Effect of quality of radiation, size of field, and depth of underlying tissue on back-scatter

3 Effect of quality of radiation, size of field, and focal-skin distance on penetration of the radiation into the tissue, or depth dose.

4 Isodose charts Determination of radiation intensity in roentgens, and quality in half-value layer and effective wave length

5 Scattering and total absorption of photons in the tissue

6 Discussion of the record sheet as recommended by Standardization Committee of the Radiological Society of North America

Courses No 24 and 29 Thursday and Friday
8 30-10 A M

Radiotherapy of Cancer of the Pharynx and Larynx

MAURICE LENZ, M.D

New York, N Y

(This course requires two days)

The result of radiotherapy in cancer of the pharynx and larynx is influenced chiefly by the extent, localization, and inherent radiosensitivity of the cancer, by the radioresistance of the irradiated normal tissues, and by the adequacy of the tumor dosage. The administration of adequate tumor dosage is facilitated by the infrequency of distant metastases of most of these cancers, it is rendered more difficult by the tendency of the cancers to silent regional lymph node involvement and extension to the laryngeal cartilages and base of the skull. This involvement of cartilage and bone, as well as their invasion by the ever-present pharyngeal infection lowers the radiosensitivity of these irradiated normal structures and interferes with the administration of adequate tumor dosage.

The various factors mentioned above, including technic of radiotherapy, will be discussed informally on the basis of reports in the literature and personal observations during the past twenty years at the Presbyterian, Manhattan Eye, Ear, Nose and Throat, and Montefiore Hospitals, New York.

Course No 25 Friday, 8 30-10 A M

Diseases of the Gallbladder with Remarks on Cholangiography and Pertinent Pancreatic Disorders

WENDELL G SCOTT, M.D

Washington University School of Medicine
St Louis Mo

This course includes a brief summary of the development and the technics of cholecystography with a present-day appraisal of the intravenous and oral methods, using compounds of tetraiodophenol

phthalein and of the chemical, iodoalphonic acid (Priodax)

Included in this course is a discussion of the uses of fatty meals and an evaluation of cases with delayed emptying of the gallbladder. There will be a review of experience in evaluating the clinical significance of faint concentrations of the compound in the interpretation of cholecystograms.

The indications for cholangiography and the technics as employed at the Washington University School of Medicine will be presented for discussion, along with those employed elsewhere.

An accurate and objective method for the diagnosis of pancreatic disease is still lacking and presents a challenging problem for solution. A few of the radiographic procedures that are employed in the diagnosis of pancreatic diseases will be demonstrated in the discussion of this problem.

Course No 26 Friday, 8 30-10 A M

Congenital Obstructive Lesions of the Alimentary Tract

JOHN CAFFEY, M.D

The Presbyterian Hospital
New York, N Y

Morbid anatomy, roentgen findings and their evaluation in

Atresia of the esophagus

Hypertrophic pyloric stenosis

Obstructions of the small intestine due to

Congenital volvulus

Failure of recanalization

Pertoneal bands

Duplications

Meconium ileus

Atresia of the colon and megacolon

Rectal atresia

Special emphasis will be placed on hazards of barium in some cases and the value of plain 3 position films of the abdomen

(See also Course No 21)

Course No 27 Friday, 8 30-10 A M

Classification, Diagnosis, and Treatment of Benign Lesions of the Female Genital Tract

JAMES A CORSCADEN, M.D

New York, N Y

Myomata of the uterus are composed of tissue which requires no treatment. They become clinically significant because of size, symptoms, and changes in the tumor. Uterine bleeding is the principal symptom. Its nature should always be established by a diagnostic curettage whatever treatment is carried out. Treatment of fibroids is either by observation, by operation, or by induction of the menopause by irradiation of the ovaries. The choice of treatment depends upon its effect on sym-

toms and on the local lesion, its efficacy as a prophylactic measure, and upon the associated injury to the patient

Endometrial and cervical mucous polyps are treated by excision

Ovarian enlargements are either (1) dysfunctional cysts, (2) endometriosis, or (3) neoplasms. Neoplasms should always be removed. Endometriosis may be treated conservatively but is often operated upon. Dysfunctional cysts rarely require treatment. Their removal seldom affects symptoms.

Course No 28 Friday, 8 30-10 A M

Diagnosis and Treatment of the Lymphoid Tumors

HUGH F HARE, M.D

Lahey Clinic
Boston, Mass

This is a discussion of diagnosis of the lymphoid tumors and of the indications and contraindications for treatment with the various types of therapy

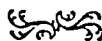
Course No 29 Friday, 8 30-10 A M

Radiotherapy of Cancer of the Pharynx and Larynx

MAURICE LENZ, M D

New York, N Y

(Continued from Thursday See Course No 24)



ANNOUNCEMENTS AND BOOK REVIEWS

SECTION ON RADIOLOGY CALIFORNIA MEDICAL ASSOCIATION

At the 76th Annual Meeting of the California Medical Association, recently held in Los Angeles, the following officers were elected by the Section on Radiology: Chairman, D R MacColl, M D, Los Angeles, Secretary, Sydney F Thomas, M D, Palo Alto Clinic, Palo Alto

FLORIDA RADIOLOGICAL SOCIETY

At the last meeting of the Florida Radiological Society, Dr J Maxey Dell, Jr of Gainesville was elected President, Dr James F Pittman of Lake City, Vice President, and Dr J A. Beals of Jacksonville, Secretary-Treasurer. The Society will hold its next meeting in November

OHIO STATE RADIOLOGICAL SOCIETY

The new officers of the Ohio State Radiological Society are: Dr Ralph Holmes, Chillicothe, President, Dr Henry Snow, Dayton, Vice-President, Dr Carroll Dundon, Cleveland, Secretary-Treasurer, Dr H F Fulton, Columbus, and Dr E C Elsey, Cincinnati, are the new members of the Executive Committee, and Dr Clarence Hufford, Toledo and Dr Harold Reineke, Cincinnati, Councilors to the American College of Radiology, for the Northern and Southern Districts, respectively

The 1948 meeting of the Society will be held in conjunction with the meeting of the Ohio State Medical Association in Cincinnati in May 1948

TEXAS RADIOLOGICAL SOCIETY

The next meeting of the Texas Radiological Society will be held Jan 17, 1948 in Temple, Texas. Dr C A Stevenson, of Temple, is President of the Society and Dr R P O'Bannon, of Fort Worth, is Secretary

PROFESSOR ROBERT KIENBOCK

On March 28, 1947, Prof Robert Kienböck, of Vienna was made an honorary member of the Society of Physicians of that city, and in public session presented with a diploma attesting to this honor. Following this presentation Professor Kienböck spoke briefly, reviewing his life's work, paying tribute to his teachers in many scientific and medical centers of Western Europe and the friendship and inspiration received from many contemporaries in medicine, particularly in radiology

Professor Kienböck undoubtedly is one of the pioneers of radiology who in close contact with others, particularly the late Professor Holznecht, established roentgenology as a specialty in Vienna and

Austria. As a charter member of the Viennese and Austrian Roentgen Ray Societies, as a teacher at the University of Vienna, in numerous lectures and demonstrations at that University, and in many another European medical center, he presented over a period of many years the results of his extensive roentgenological and clinical studies which encompassed the entire field of radiology, as that specialty came to play an increasingly important part in modern medicine

Many of Professor Kienböck's publications are classical contributions to radiology. Malacia of the lunette bone usually carries his name. His studies on the effect of radiation on skin, governing the treatment of skin diseases, his concepts of the treatment of neoplastic disease and the diagnosis of trophic osseous degeneration on a nutritional basis, and observations on echinococcus, multiple neuroma, inflammatory pericardial diverticula, malignant metastatic disease involving the skeleton, all attest to his knowledge, judgment, and sagacity

After 1938 Professor Kienböck encountered increasing handicaps in his scientific work, which in 1943 he had to relinquish entirely, though a number of important studies concerning, for instance, chondromatosis and sarcomatosis of skeletal structures, bone tumors, xanthomatosis, scurvy, osteosclerosis, etc., were in preparation

The Radiological Society of North America, of which Professor Kienböck is a Corresponding Member, congratulates him on the honors recently bestowed upon him. It is hoped that with more settled conditions in Vienna, further scientific contributions from his pen may be forthcoming

Books Received

OSTEOTOMY OF THE LONG BONES By HENRY MILCH, M D, Consulting Orthopedist, Maimonides Hospital. Attending Orthopedic Surgeon, Hospital for Joint Diseases and Riverside Hospital, New York. Fellow of the American Academy of Orthopedic Surgeons, the American College of Surgeons, and the New York Academy of Medicine. A volume of 294 pages, with 181 illustrations. Published by Charles C Thomas, Springfield, Ill. 1947. Price \$6.75

CANCER DIAGNOSIS, TREATMENT, PROGNOSIS By LAUREN V ACKERMAN, M D, Pathologist to the Ellis Fischel State Cancer Hospital, Assistant Professor of Pathology, Washington University School of Medicine, St. Louis, Mo. and JUAN A DEL REGATO, M D, Radiotherapist to the Ellis Fischel State Cancer Hospital, former Assistant to the Radium Institute of the University of Paris. A volume of 1200 pages with 749 illustrations, 42 in color on nine plates. Price \$20.00

LA TOMOGRAFIA, NELLE MALATTIE DEI SENI PARANASALI CONTRIBUTO CLINICO RADIOLOGICO By ENRICO BOZZI, Docente, Primario di Otorinolaringoiatria dell'Ospedale Civile di Monza, and LUDOVICO MUCCHI, Docente, Dirigente la Sez Radiol della Clinica Chirurgica dell'Università di Milano A volume of 152 pages with 140 illustrations Lincinio Cappelli, Bologna, 1947

Book Reviews

ROENTGEN INTERPRETATION By GEORGE W HOLMES, M D, Board of Consultation, Massachusetts General Hospital and Clinical Professor of Roentgenology Emeritus, Harvard Medical School, and LAURENCE L ROBBINS, M D, Radiologist in Chief to the Massachusetts General Hospital and Associate in Radiology, Harvard Medical School A volume of 398 pages, with 266 illustrations Published by Lea & Febiger, Philadelphia, 7th edition, 1947 Price \$7 00

This new edition of *Roentgen Interpretation* is the seventh of a well seasoned and thoroughly reliable textbook which was first published in 1919 under the authorship of Dr George W Holmes and the late Dr Howard E Ruggles It is pleasing to note that Dr Robbins has become the new joint author, thus assuring continuance of this excellent work with the same high scholastic standards that have marked earlier editions

The text is concise but unusually comprehensive for a book of this size All parts of the body are considered but some pathologic conditions are omitted and some are dealt with rather briefly The material has been revised and brought up to date in the light of newer roentgen findings which have proved their soundness A beginning has been made, also, in changing the illustrations from the previous positive reproductions to the more desirable negative ones It is regrettable that it was not possible to make this change over complete but, as the authors explain in their preface, there were serious obstacles in the way A comprehensive bibliography follows each chapter There is no question that the text will continue to be invaluable as a ready reference volume to students who are interested in radiology

SURFACE AND RADIOLOGICAL ANATOMY FOR STUDENTS AND GENERAL PRACTITIONERS By A B APPLETON, W J HAMILTON, AND IVAN C C TCHAPEROFF Second edition rewritten by A B APPLETON M A M D (Cantab), Professor of Anatomy in the University of London and Director of the Department of Anatomy in the Medical School of St Thomas's Hospital, London, former Fellow of Downing College, Cambridge, W J HAMILTON, M D, D Sc, F R S E Regius Pro

fessor of Anatomy in the University of Glasgow, formerly Professor of Anatomy in the University of London at the Medical College of St Bartholomew's Hospital, and G SIMON, M D, B Ch, D M R E (Cantab), Demonstrator of Radiological Anatomy in the Medical College of St Bartholomew's Hospital, and Assistant Radiologist to the Diagnostic X-ray Department, St Bartholomew's Hospital, London A volume of 332 pages, with 390 illustrations Published by The Williams & Wilkins Co, Baltimore, 1946 Price \$7 00

Surface and Radiological Anatomy, by Appleton, Hamilton, and Tchaperoff, at the time of its original publication in 1938 was one of the first books dealing primarily with anatomy in which the radiological appearances of normal structures were given a significant place in the text The work has now been rewritten and published in a second edition, with Dr Simon replacing Dr Tchaperoff in the group of authors As its title implies, it is devoted to the study of surface anatomy and the role of radiology in such a study

The text is introduced by a chapter on General Anatomy and Methods, following which the parts of the body are taken up in order An Appendix gives the approximate dates of the appearance of the various centers of ossification and union of the epiphyses, as well as tables showing the segmental innervation of the muscles of the upper and lower limbs

The plan of treatment may be illustrated by the section on the shoulder, which embraces the following headings and subheadings

- Surface Contours
- Landmarks on Thoracic Skeleton
- Skeleton of the Shoulder Region
- Superficial Muscles
- Movements
 - Sternoclavicular Joint
 - Scapula
 - Shoulder Joint
- Radiology
 - Clavicle
 - Sternoclavicular Joint
 - Shoulder Joint
 - Development from Birth to Adolescence

The relation of surface contours to the underlying structures is demonstrated by retouched photographs and sketches, along with roentgenograms of the corresponding areas

This volume should be of considerable aid in a rapid review of the surface and underlying gross anatomy of various areas which are being studied roentgenographically It will find a welcome place in the library of radiologists and students of anatomy alike

RADIOLOGICAL SOCIETIES SECRETARIES AND MEETING DATES

Editor's Note Secretaries of state and local radiological societies are requested to cooperate in keeping this section up-to date by notifying the editor promptly of changes in officers and meeting dates Address Howard P Doub, M D The Henry Ford Hospital, Detroit 2, Mich

UNITED STATES

RADIOLOGICAL SOCIETY OF NORTH AMERICA *Secretary-Treasurer* Donald S Childs M D 607 Medical Arts Bldg, Syracuse 2 N Y

AMERICAN RADIUM SOCIETY *Secretary* Hugh F Hare M D, 605 Commonwealth Ave, Boston 15 Mass

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Arkansas

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CONNECTICUT STATE MEDICAL SOCIETY SECTION ON RADIOLOGY *Secretary* Robert M Lowman, M D, Grace-New Haven Hospital Grace Unit, New Haven Meetings bimonthly second Thursday

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ILLINOIS RADIOLOGICAL SOCIETY *Secretary-Treasurer*, William DeHollander M D, St Johns' Hospital, Springfield Meetings quarterly as announced

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY *Secretary* Frank S Hussey, M D, 250 East Superior St Chicago 11

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ORLEANS PARISH RADIOLOGICAL SOCIETY *Secretary*, Joseph V Schlosser, M D, Charity Hospital of Louisiana, New Orleans 13 Meets first Tuesday of each month

SHREVEPORT RADIOLOGICAL CLUB *Secretary*, Oscar O Jones, M D, 2622 Greenwood Road Meets monthly September to May, third Wednesday, 7 30 P M

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ST LOUIS SOCIETY OF RADIOLOGISTS *Secretary* Edwin C Ernst, M D, 100 Beaumont Medical Bldg Meets on fourth Wednesday of each month, October to May

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New England

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New Jersey

RADIOLOGICAL SOCIETY OF NEW JERSEY *Secretary*, Raphael Pomernitz, M D, 31 Lincoln Park New-

ark 2 Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called

New York

ASSOCIATED RADIOLOGISTS OF NEW YORK, INC *Secretary*, William J Francis, M D, East Rockaway, L I

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Oklahoma

OKLAHOMA STATE RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Peter M Russo, M D, 230 Osler Building, Oklahoma City Meetings three times a year

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Pennsylvania

PENNSYLVANIA RADIOLOGICAL SOCIETY *Secretary Treasurer*, James M Converse M D , 416 Pine St , Williamsport 8 Meets annually

PHILADELPHIA ROENTGEN RAY SOCIETY *Secretary*, Calvin L Stewart M D , Jefferson Hospital, Philadelphia 7 Meets first Thursday of each month at 8 00 P M from October to May in Thomson Hall College of Physicians, 21 S 22d St

PITTSBURGH ROENTGEN SOCIETY *Secretary Treasurer*, Lester M J Freedman, M D 415 Highland Bldg , Pittsburgh 6 Meets second Wednesday of each month at 6 30 P M October to May, inclusive

Rocky Mountain States

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Maurice D Frazer, M D , Lincoln Clinic Lincoln, Nebr

South Carolina

SOUTH CAROLINA X-RAY SOCIETY *Secretary-Treasurer*, Robert B Taft, M D , 103 Rutledge Ave , Charleston 16

Tennessee

MEMPHIS ROENTGEN CLUB Meetings second Tuesday of each month at University Center

TENNESSEE RADIOLOGICAL SOCIETY *Secretary Treasurer* J Marsh Frère M D 707 Walnut St Chattanooga Meets annually with State Medical Society in April

Texas

DALLAS-FORT WORTH ROENTGEN STUDY CLUB *Secretary*, X R Hyde, M D , Medical Arts Bldg , Fort Worth 2 Meetings on third Monday of each month in Dallas in the odd months and in Fort Worth in the even months

TEXAS RADIOLOGICAL SOCIETY *Secretary Treasurer* R P O'Bannon M D 650 Fifth Ave Fort Worth 4 Next meeting Jan 17 1948

Utah

UTAH STATE RADIOLOGICAL SOCIETY *Secretary Treasurer* M Lowry Allen M D Judge Bldg Salt Lake City 1 Meets third Wednesday January March May September, November

UNIVERSITY OF UTAH RADIOLOGICAL CONFERENCE *Secretary* Henry H Lerner M D Meets first and third Thursdays September to June inclusive at Salt Lake County General Hospital

Virginia

VIRGINIA RADIOLOGICAL SOCIETY *Secretary*, E Latan Flanagan, M D 215 Medical Arts Bldg , Richmond 19

Washington

WASHINGTON STATE RADIOLOGICAL SOCIETY *Secretary Treasurer*, Homer V Hartzell, M D 310 Stimson Bldg Seattle 1 Meetings fourth Monday October through May, at College Club Seattle

Wisconsin

MILWAUKEE ROENTGEN RAY SOCIETY *Secretary-Treasurer* C A H Fortier M D 231 W Wisconsin Ave , Milwaukee 3 Meets monthly on second Monday at the University Club

RADIOLOGICAL SECTION OF THE WISCONSIN STATE MEDICAL SOCIETY *Secretary* S R Beatty M D 185 Hazel St , Oshkosh Two-day meeting in May and one day at annual meeting of State Medical Society in September

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE Meets first and third Thursdays 4 to 5 P M September to May inclusive Room 301, Service Memorial Institute 426 N Charter St Madison 6

CANADA

CANADIAN ASSOCIATION OF RADIOLOGISTS *Honorary Secretary Treasurer*, E M Crawford, M D 2100 Marlowe Ave Montreal 28, Quebec Meetings in January and June

LA SOCIÉTÉ CANADIENNE FRANÇAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES *General Secretary* Origène Dufresne M D , Institut du Radium, Montreal Meets on third Saturday of each month

CUBA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA Offices in Hospital Mercedes Havana Meets monthly

MEXICO

SOCIEDAD MEXICANA DE RADIOLOGÍA Y FISIOTERAPIA *General Secretary* Dr Dionisio Pérez Cosío Marsella 11 México D F Meetings first Monday of each month



ROENTGEN DIAGNOSIS

THE HEAD AND NECK

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Lorenzo Expósito Rev cubana pediat 18 497-508, August 1946

The author presents two cases of premature closure of the cranial sutures, in a boy of nine years and a girl of eight years. In one of the cases the manifestations were very slight from the clinical point of view but quite obvious from the radiological standpoint. In the other case the clinical manifestations of turriccephaly, exophthalmos, visual changes, and prognathism were pronounced, as well as a curious ocular displacement. The radiographic findings were characteristic. Exophthalmos is frequently very pronounced because of changes in the shape of the orbits. Dislocation of the ocular globes has been reported. In the author's second case the globes were completely dislocated at the time of the examination.

The diagnosis is easy in cases with accentuated deformities, but in the early forms the radiographic examination is indispensable. JAMES T. CASE, M.D.

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This case demonstrates that tomography is decisive in the diagnosis of infiltrating polypoid tumors situated in the inferior portion of the trachea. By this procedure the clinical diagnosis of an infiltrating and stenosing cancer, accompanied by symptoms of right recurrent nerve syndrome due to secondary adenopathy, was incontrovertibly confirmed. The tomograms are necessary not only to establish the site of the tracheal tumor but also for determining the infiltrative and polypoid nature of the lesion which provokes the tracheal stenosis. Direct radiography serves only to recognize the existence of a tracheal tumor.

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The pathological picture of these cases was classified as follows: (1) multiple cysts and a considerable amount of normally functioning lung, (2) multiple cysts with little or no normally developed lung, (3) a large amount of abnormally developed bronchial tree elements, a number of smaller cysts, and little or no normally developed terminal respiratory units.

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of investigation, especially radiology, have demonstrated the relative frequency of this process

The authors base this paper on 8 cases of non tuberculous non traumatic, spontaneous pneumothorax occurring in children under two years of age. Sex, race, and season have no influence on the affection. Violence is an important factor, childhood diseases such as whooping cough, bronchitis, and bronchopneumonia are causative agents. Previously existing parenchymal pleuropulmonary lesions predispose to the passage of air into the pleural cavities. Knowledge of the mechanism of the formation of subpleural blebs throws light on the pathogenesis of spontaneous pneumothorax.

Radiographic and fluoroscopic studies are of prime importance but occasionally may be supplemented by pleuroscopy.

Empyema is a rare complication of non-tuberculous spontaneous pneumothorax.

JAMES T. CASE, M.D.

Bilateral Pulmonary Infarction and Pneumothorax Complicating Hypertensive Coronary Heart Disease with Myocardial Infarction. Report of a Case. H. Milton Rogers. *Am Heart J* 32: 519-528, October 1946.

The author reports a case of bilateral spontaneous pneumothorax associated with pulmonary infarction, in a patient with hypertensive heart disease followed by coronary thrombosis and occlusion of the left anterior descending coronary artery with myocardial infarction. A 44 year old white man gave a history of hypertension for ten to twelve years. Examination following an acute episode showed an elevation of temperature, an increased white count, and albumin in the urine. The electrocardiogram revealed anterior myocardial infarction. Roentgen findings were suggestive of pulmonary infarction, but a bronchopneumonia could not be excluded. Treatment was instituted and most of the symptoms abated. Within a few days however, there was another rise in temperature and a roentgen examination of the chest revealed a bilateral pneumothorax, with severe passive congestion in both lungs and probable infarction in the lower lobes. Nine days later another acute episode set in, with pain in the right upper quadrant, sudden elevation of temperature, and albuminuria, leading to a diagnosis of infarction of the right kidney, probably secondary to embolization of the right renal artery. Following recovery from this attack, roentgenograms of the chest showed clear lung fields with resolution of the infarcts. Two months later symptoms of right heart failure were evident. The patient was again hospitalized, and dicumarol therapy was instituted in addition to the usual cardiac measures. Roentgen studies of the chest now revealed bilateral pulmonary congestion and an increase in heart size. Death ensued from right heart failure five weeks later, 130 days after the original examination.

Necropsy revealed an enlarged heart, weighing 600 gm., a left ventricular aneurysm, a well organized thrombus in the left ventricle which measured $6 \times 5 \times 2$ cm., adherent to the endocardium beneath the aneurysm, small old mural thrombi in the right ventricle, coronary sclerosis of the left circumflex and the right coronary artery (grade 2) sclerosis (grade 3) of the left anterior descending coronary artery, which contained an old antenatal thrombus originating 1 cm from the bifurcation of the left coronary artery, a small pleural cyst over the right middle lobe containing an organized

blood clot, atelectasis of the right lower lobe, which contained an organized infarct measuring $4 \times 4 \times 3$ cm., smaller infarcts in the right middle and left lower lobes, well organized thrombi in the pulmonary arteries leading to the right middle and lower lobes, atrophy of the right kidney, most of which was destroyed by old and recent infarcts, narrowing of the right renal artery by atherosclerotic plaques.

The author concludes that spontaneous bilateral pneumothorax may occur in association with pulmonary infarction and that secondary infection of an infarct is not essential for the development of this complication. The exact mechanism of the pneumothorax in the case recorded is not entirely clear. It is suggested that it may have been the result of rupture of the alveoli of the lung during coughing, permitting passage of air into the interstitial tissues.

Special attention is drawn to two clinical features of the case: (1) the marked elevation of the diastolic pressure following the renal infarction, and (2) the absence of further intracardiac or peripheral manifestations of vascular thrombosis after the institution of dicumarol therapy.

HENRY K. TAYLOR, M.D.

Spontaneous Pneumothorax. Report of a Case. John W. Hope and Alva C. Surber, Jr. *U S Nav M Bull* 46: 1600-1603, October 1946.

The authors report a case of spontaneous pneumothorax developing in a sailor aboard a heavy cruiser engaged in a very active and difficult operation in the Pacific. The case is presented not because of its medical rarity but to show what can be done with limited equipment. The only x-ray facility aboard was a General Electric dental unit and this was used for various x-ray examinations. The technique of taking a chest film was relatively simple. The machine was firmly attached to the bulkhead in such a position that it could be swung to the dental chair. When employed for chest work it was swung as far out into the dental office as possible and brought down to the level of the chest to be examined. The patient was seated with his back to the machine on a high surgical stool 72 inches from the x-ray tube, and the cassette was held in front of him by a hospital corpsman. Since the dental unit was fixed at 10 ma and 85 kv, the time was the only variable. The time employed on the average chest was one second. A different hospital corpsman was used each time to avoid overexposure to radiation. The x-ray findings in this case confirmed the clinical impression of a left-sided pneumothorax. The patient was treated symptomatically and was able to return to light duty fifteen days after the occurrence of the pneumothorax. A chest roentgenogram a week later was normal.

A Pulmonary Reaction Following Intrabronchial Instillation of Lipiodol in Bronchial Asthma. S. I. Kooperstein and H. E. Bass. *Am J Roentgenol* 56: 569-576, November 1946.

Experience has shown that the use of iodized oil in the bronchopulmonary tree may be accompanied by some danger. A fatality was reported by Macdonald (*Ann Int Med* 6: 253-277, 1932) following bronchography with lipiodol. The patient was a child who had suffered from asthmatic attacks.

In a recent study of 40 cases of bronchial asthma, bronchograms were obtained as part of a clinical investigation, with lipiodol as the contrast medium. In

peatedly negative sputum should rule out the diagnosis of tuberculosis

(5) Intrathoracic pressure changes due to large cysts of the lungs may be mistaken for spontaneous pneumothorax. The differential diagnosis can usually be made by establishing a pneumothorax thus demonstrating the cyst wall or by injecting an opaque medium, such as iodized oil, into the cystic space and visualizing the cyst wall and trabeculae roentgenographically

(6) A history of an insidious onset of a pulmonary suppurative process in a child without the usual etiologic factors for the production of bronchiectasis or lung abscess should strongly suggest congenital cystic disease rather than pneumonitis

(7) Continued cough in children or young adults without obvious cause should be looked upon with suspicion, and repeated fluoroscopic and roentgenographic examination should be made for evidence of the lesion

The authors emphasize the fact that the symptomatology, physical findings, laboratory findings, and even x-ray studies may be very confusing and that other conditions are often suspected for long periods of time before the true diagnosis is made

BERNARD S. KALAJIAN, M.D.

How Can We Differentiate, on the Appearance, Apparently Benign Intrathoracic Tumors? A. Brunner, *Schweiz med Wchnschr* 76 1013-1014 Oct 5, 1946

In a discussion of the differential points between benign and malignant intrathoracic tumors the author makes the point that it is impossible on the basis of a single roentgen examination to differentiate conclusively between them, while observation and serial study may in many cases clarify the picture, exploratory thoracotomy is recommended in those cases in which doubt persists after a reasonable time. Illustrative case reports are included

LEWIS G. JACOBS, M.D.

Primary Amyloidosis of the Lungs Paul R. Dirkse, *Am J Roentgenol* 56 577-585 November 1946

Primary amyloidosis is an uncommon disease and is seldom diagnosed clinically. The author quotes the criteria established by Lubarsch for its differentiation from the more common secondary form. These include almost complete absence of amyloid from the organs usually involved in secondary amyloidosis as the spleen, liver, and kidneys, presence of amyloid in organs and parts not usually involved as heart, lungs and skin, absence of a preceding or concomitant disease to which the presence of amyloidosis can be ascribed. The tongue is a frequent site of involvement. Extensive deposits in the heart may lead to cardiac failure. Gastrointestinal deposits may result in either constipation or diarrhea, abdominal pain or vomiting. Deposits in bone are rare. Skin lesions may be lichenoid or plaque-like hyperkeratoses. Infiltrative lesions have been found roentgenographically in the stomach and the colon.

In the case reported by the author the first roentgenogram, twenty months before death, already showed some bilateral enlargement of the hilar shadows and a linear and finely nodular peritruncal infiltration widely disseminated in the parenchyma of the lungs. Seven months later a left basilar pleuritis developed. One year after the first examination a gradual progression of

the hilar and parenchymal fibrosis was shown. There was also some atelectasis in the left base. These changes slowly progressed in degree and extent and two months before death there was beginning heart failure. The similarity to pulmonary sarcoidosis was striking. Histologic examination showed deposits of amyloid in the alveolar walls and lung septa. Blood vessel walls were filled with amyloid. There was almost solid infiltration of mediastinal connective tissue. The normal structure of the lymph nodes was replaced by large deposits of amyloid. There were deposits also in the jejunum, the spleen, and the heart.

Dyspnea was a prominent feature and there was a history of some indefinite abdominal discomfort, diarrhea, and fatigability.

CLARENCE E. WEAVER, M.D.

Roentgenological Aspects of Primary Atypical Pneumonia. Wayne K. Cooper, *J Iowa M Soc* 36 487-489 November 1946

Cooper believes that roentgenographic manifestations of primary atypical pneumonia may be resolved into three groups: (1) widening or blurring of bronchovascular markings in part of a lobe or lobes, (2) diffuse increase in density of part of one or more lobes with bronchovascular markings still visible through the increased density, (3) a combination of (1) and (2). The definite diagnosis depends on the x-ray appearance and the latter is highly reliable particularly in epidemics, although differentiation of this type of pneumonia from bacterial lobar pneumonia, bronchiectasis, and tuberculosis offers difficulty in some cases. Cooper concludes that roentgen therapy, as reported by others, is a beneficial therapeutic agent which should be utilized more frequently.

ELLWOOD W. GODFREY, M.D.

Pulmonary Infiltrations with Associated Eosinophilia. Forrest M. Willett and Elliot Oppenheim, *Am J M Sc* 212 608-612, November 1946

Loeffler described the syndrome of transitory pulmonary infiltration associated with eosinophilia. The main characteristic of these infiltrations was their sudden appearance and disappearance in three to eight days. Cases with severe symptoms and a chronic course have however been described in which the pulmonary infiltrations could be demonstrated roentgenologically for weeks or months.

While the pulmonary infiltrations in many of these cases are probably on an allergic basis, they have also been associated with such diseases as trichinosis, brucellosis, amebiasis, ascariasis, and coccidioidomycosis. In coccidioidomycosis the eosinophilia has usually been slight, ranging from 5 to 18 per cent.

Two cases of coccidioidomycosis are reported in detail. In the first case with dissemination, the pulmonary infiltration lasted about sixty-seven days and the eosinophilia ranged from 6 to 89 per cent. In the second case the infiltration lasted about forty-six days and the eosinophilia ranged from 2 to 27 per cent.

BENJAMIN COLEMAN, M.D.

Non-Tuberculous Spontaneous Pneumothorax in Early Infancy. José Díaz Rousselot and Roberto Valdés Díaz, *Rev cubana pediat* 18 199-230 April 1946

Spontaneous pneumothorax has long been considered as a rare condition in early infancy. Modern methods

the fourth day after birth X ray examination of the esophagus with iodized oil introduced through a catheter showed the upper segment extending to the level of the second dorsal vertebra Air in the gastro-intestinal tract indicated a communication between the trachea and the lower segment Immediate operation was undertaken, the approach being through the right posterior area Both upper and lower segments were identified, separated by only a short distance The lower segment was attached to the trachea about 0.5 cm inferior to the lower end of the upper segment The fistula connecting the lower segment was ligated and anastomosis of the esophagus was done over a No 8 French urethral catheter passed into the stomach and up into the mouth A double row of very fine silk sutures was used and the catheter was removed through the mouth The postoperative régime included prophylactic penicillin administration and supportive fluid and nutritive therapy The wound healed by primary intention Repeated x ray examination on and after the third postoperative day showed no stricture at the site of anastomosis The infant developed normally and nine months after the operation weighed 16 pounds, 4 1/2 ounces

In discussion of the case, the authors express the opinion that the right extrapleural posterior approach is the easiest They inserted no drain at the site of the anastomosis, but aspirated the closed extrapleural space daily for five days, injecting penicillin after each aspiration They believe that a higher level of penicillin may thus be maintained in the wound

The three important points in the postoperative care are (1) the prevention of infection, (2) the control of body temperature, (3) the maintenance of nutrition

J E WHITELEATHER, M D

Treatment of Esophageal Achalasia or Cardiospasm Report of Four Patients Treated Surgically H Max Schiebel Surgery 20 558-570, October 1946

The syndrome of achalasia or cardiospasm has been recognized since 1679 The symptoms are pain, dysphagia, and regurgitation of food Cold drinks and cold foods are most poorly tolerated Loss of weight, vomiting and remissions and exacerbations may frequently be seen These may be associated with emotional conflicts, but not necessarily so X-ray studies usually show an olive tip type of obstruction with or without dilatation of the esophagus Accumulated food and secretions make the examination difficult, and lavage of the esophagus may be necessary as a preliminary measure

The dilatation may be flask-shaped, fusiform, or S-shaped (sigmoid) These types probably represent variations in the degree of dilatation and lengthening of the esophagus following its obstruction and must be taken into consideration in determining upon the method of treatment

The major complication of the condition is pulmonary infection due to regurgitation of food and aspiration into the respiratory tract This occurs sometimes at night without the patient's knowledge simply as an overflow Other complications are emotional instability, bleeding and chronic cough Death from starvation has occurred

Simple measures such as warming of food, thorough mastication, slow eating, rest before and after meals prove effective in some cases In others dilatation may be done with good results Surgical intervention is in-

dicated under the following conditions (1) When roentgenographic examination discloses increased length of the esophagus with a sigmoid or flask-shaped contour In these cases, dilatation is difficult, dangerous, and must usually be kept up more or less continuously (2) When, under proper care as to rest, types of food, and reasonable freedom from simple emotional disturbance, frequent dilatation is required (once a week or several times a month) Under such circumstances the patient should be advised that an operative procedure is available which carries a high percentage of cure (3) When the patient does not tolerate dilatation well because of fear and pain and has no possibility of learning the use of bougies without medical aid (4) When the patient is geographically or financially unable to have frequent dilatations

Surgical treatment consists in esophagogastrostomy, according to the technic described by Ochsner (Surg, Gynec & Obst 72 290, 1941), through a transperitoneal approach A double layer anastomosis is accomplished Four cases thus treated are recorded In 2 there was a complicating wound infection with *Staphylococcus albus* and mixed organisms In one, the drainage persisted for several months, necessitating re-drainage In this case, contamination by stomach contents was felt to be responsible for the infection In neither of these cases, however was the function of the esophagogastrostomy impaired All 4 patients were completely relieved of symptoms

J E WHITELEATHER, M D

Esophageal Hiatus Hernia. Louis L. Perkel J M Soc New Jersey 43 414-417, October 1946

The author reviews the general features of esophageal hiatus hernia, including the important roentgen signs, and presents his own series of 51 cases, observed in the course of 7,500 gastro-intestinal roentgen examinations The average age of his patients was 63.5 years and the ratio of females to males was 5 to 1 The symptoms simulated cardiac, gastric, or cholecystic disease in 86 per cent of the cases In 56 per cent the condition was misdiagnosed as either gallbladder or coronary disease Great stress is placed upon the roentgen examination, especially in the horizontal position

Preclinical Stage of Infantile Hypertrophic Pyloric Stenosis. Arvid Wallgren Am J Dis Child 72: 371-376 October 1946

Since hypertrophic pyloric stenosis does not usually appear before the age of three weeks the question arises whether the condition or the muscular hypertrophy which is its basic anatomic cause is or is not congenital In order to determine this point 1,000 newborn boys from the Göteborg Maternity Clinic (Sweden) were examined roentgenographically and subsequently kept under observation for evidence of pyloric stenosis According to Swedish statistics which show an incidence of one case in every 150 male children 6 cases might be expected from the present series Actually 5 cases developed, showing the usual clinical and roentgen signs The latter have been described by Runström (Acta paediat 26 383, 1939) as including obstruction of the pyloric canal so that its lumen is only a few millimeters in width for a distance of 2 or 3 cm, a delay in gastric evacuation time, and distention of the stomach

The significant finding in the author's study was that

3 cases, an acute febrile illness developed following the introduction of the medium, associated with roentgen evidence of pulmonary infiltration. Two of the 3 patients had a skin eruption resembling hives following bronchography, and in all 3 bilateral basal pneumonia developed nine, twelve, and ten days, respectively, following that procedure. Two patients showed a striking elevation of the total eosinophile count. Sensitivity tests in these cases seemed to incriminate the lipiodol as the agent responsible for the acute pulmonary episodes. That the iodine portion of the lipiodol was the allergen involved seemed to be borne out by the failure of these patients to react to pure poppyseed oil or butyn sulfate (the anesthetic used), and by the marked reaction produced by diodrast an organic compound of iodine. The importance of skin testing individuals, especially those with allergic backgrounds, is emphasized.

CLARENCE E. WEAVER, M D

Roentgenologic Diagnosis of Certain Congenital Lesions of the Heart and Great Vessels. David G. Pugh. *Am J Med Sc* 212: 628-635, November 1946.

This paper is a review of the more recent literature on the roentgen diagnosis of congenital cardiovascular lesions that are amenable to surgical treatment—patent ductus arteriosus, tetralogy of Fallot, coarctation of the aorta.

Roentgenologic Kymographic Studies of the Heart in the Presence of an Arteriovenous Fistula and Their Interpretation. Emile Holman. *Ann Surg* 124: 920-932, November 1946.

Arteriovenous fistulas of sufficient caliber produce cardiac enlargement and increased blood volume. Closure of such fistulas commonly produces further distention of the heart, increase in blood pressure, and slowing of the pulse. To understand more clearly the latter changes the author has made an exhaustive study of a male patient with a large arteriovenous fistula of the popliteal vessels, before and after successful surgical closure.

Kymography of the heart was done prior to operation with the fistula closed during one-half of each ten second exposure and open the other half. By careful study of the individual frames of the kymogram, it was possible to determine the exact time at which the fistula was closed by digital pressure. With the fistula closed the right auricle was reduced in size, the aorta was greatly distended, the pulmonary conus was reduced in size, and the left ventricle was distended. When the fistula was open, the right auricle and pulmonary conus resumed their distended condition and the aorta and left ventricle were decreased in size. These variations in the size of the chambers and central vessels of the heart are explained as follows:

Closing the fistula forces into the general arterial circulation the blood that formerly leaked through the fistula into the capacious venous system. With the increased blood volume present the entire arterial circulation becomes distended and remains so for a period of twenty four to thirty-six hours until the excess volume of blood is partially eliminated. The size of the heart is gradually reduced to normal except for some residual hypertrophy developing during the life of the fistula. This reduction in heart size is shown strikingly in teleroentgenograms of the author's patient. Before operation the heart measured 15.3 cm. in transverse

diameter, twenty days after operation, 14.2 cm., and ninety-six days after operation, 12.3 cm.

The retardation of the pulse following closure of the fistula is explained by the author as due to the shift of the abnormally large blood volume into the arterial circulation. He shows sudden distention of the aorta on the kymogram when the fistula is manually closed. This abnormal distention stimulates the end organs of the depressor (vagus) nerve, with immediate slowing of the cardiac contraction rate to compensate for the excessively high blood pressure incident to over distention of the arterial bed. In the following hours and days, as the blood volume is reduced, the pulse rate and blood pressure return to normal except that the diastolic pressure may remain slightly elevated.

B. S. KALAYJIAN, M D

Aneurysm of the Descending Thoracic Aorta. Samuel A. Loewenberg and Samuel Baer. *Am Heart J* 32: 653-658, November 1946.

The authors give the case history and postmortem findings for a colored male aged 61, who died of a ruptured syphilitic aneurysm. The aneurysm was located in the lower portion of the thoracic aorta, and diagnosed before death. The sacculation displaced the esophagus anteriorly and to the left and eroded the bodies of D9 and D10.

The case is reported because of the infrequent occurrence of aneurysms in the lower portion of the thoracic aorta, their varied clinical picture, and the frequency with which they remain undiagnosed during life in spite of rather characteristic clinical and roentgen findings.

HENRY K. TAYLOR, M D

Registration of the Movements of the Heart with Geiger-Müller Counters and Synchronous Electrocardiography. Gunnar Hjelmare. *Acta radiol.* 27: 334-338, May 6, 1946.

Since 1937, the author has been attempting to obtain a roentgenologic record of cardiac motion which is more exact than that obtained with the usual kymogram. The use of photo-electric cells with the fluorescent screen did not prove practical and a Geiger-Müller counter was developed for registering the heart movements during screening. An amplifier permits registration of the intensity of the incident radiation in the form of a tracing on a film strip. The counter is enclosed in a lead casing with a slit window for application at right angles over the margin of the heart to be studied. The tracing which is then superimposed upon a simultaneous electrocardiographic tracing gives the exact correlation of the motion at the studied point with the electrocardiogram. The number of cases thus far has been limited but further experiments are planned to include two Geiger-Müller counters so that motion can be recorded from two points simultaneously with the electrocardiogram.

ELIZABETH A. CLARK, M D

THE DIGESTIVE TRACT

Congenital Esophageal Atresia with Tracheoesophageal Fistula. A Case Report of Successful End-to-End Anastomosis. M. Lawrence White Jr. and McLemore Birdsong. *Surgery* 20: 548-557, October 1946.

A case of congenital atresia of the esophagus is reported. This was of the usual type (Vogt's 3 B)—a blind upper segment and a communication between the lower segment and the trachea. Diagnosis was made on

In gradual development of constriction, the intestine may be able to compensate for the obstruction, dilatation occurs but ileus is not present. A point is reached, however, where physiologic compensation cannot continue, decompensation results and ileus occurs. But, while it adapts itself well to slowly developing distention, the intestine is vulnerable to rapid distention.

Paralytic ileus may be initiated by a number of causes. Of these, the author mentions generalized purulent peritonitis, extra intestinal conditions such as pneumonia or spinal injury, and hypoproteinemia. A paralytic ileus may develop as a complication of mechanical ileus, and is frequently associated with hypoproteinemia. Protein depletion often exists with gastro-intestinal disorders, and may be aggravated by the inability of patients with ileus to take food. Redistention of the intestine along the Miller-Abbott tube may be taken as suggestive of hypoproteinemia. Whatever the immediate cause of the ileus it seems reasonable to conclude that in some way the operation of the parasympathetic nervous system is interfered with. In hypoproteinemia, the interference seems to be associated with edema of the intestinal wall. In these cases x-ray examination of the chest may show edema of the lungs.

The effect of adhesions on the wall of the intestine is a little more complex than mere mechanical pressure. The narrowing at the site of the adhesions must be due to a contraction of the circular muscle and not to pressure from the outside. It seems that both a localized acute inflammation and a fibrotic process in the wall at the site of an adhesion are capable of producing a localized disturbance in the motor physiology of the intestine, manifested by narrowing. This narrowing may persist after death. The author speculates on the possibility of a fibrosis resulting in the intestinal wall, following a long continued ischemia at the site of contraction. It seems possible that a mechanical stimulus from the pull of the peristaltic contraction transmitted caudad through the adhesions to the wall ahead of the peristaltic wave may play a part in causing the localized narrowing. This would have somewhat the same effect as is noted in pinching the intestine.

This paper is an excellent treatise on the normal and morbid physiology of the small intestine.

CLARENCE E. WEAVER, M.D.

Barium as a Factor in Intestinal Obstruction. Leonard K. Stalker. *Am J Surg* 72: 756-757, November 1946.

The author presents the case of a 71 year-old woman who for about two weeks suffered vague abdominal pains associated with indefinite dyspepsia. Physical examination was negative and a barium meal was given. Within twelve hours a nearly complete intestinal obstruction developed, which was relieved by prolonged intestinal suction supportive therapy and in one week elective surgery. Operation revealed a 'napkin ring' type carcinoma at the hepatic flexure with some barium still present in the small intestine and proximal colon.

It is pointed out that in patients in whom there is any possibility of an obstructing lesion of the lower intestinal tract, roentgen study with retrograde barium would be safer than oral administration. Lesions of the right half of the colon are particularly apt to be relatively symptomless because of the semifluid state of the fecal matter in this region. When barium is given by mouth

in cases such as the one presented, one risks the precipitation of a complete obstruction.

PAUL W. EYLER, M.D.

Pneumoperitoneum in a Newborn Child Due to Perforation of the Ileum. Laudelino H. González. *Rev cubana pediat* 18: 445-452, July 1946.

The rarity of reports of perforation of the intestinal tract in the newborn and the exceptional cure of such perforation led the author to record the present case. He mentions another case from his clinic with double perforation of the transverse colon and peritonitis.

The published literature indicates that of all perforations occurring in the gastro intestinal tract, whether in intrauterine life or in the postnatal period, the majority involve the ileum. Meconial impaction is the most common cause as was first observed by Andersen (*Am J Dis Child* 56: 344, 1938). In some cases there has been associated pancreatic fibrosis or biliary duct obstruction to explain the meconial hardening, but in others there has been found no alteration either in the pancreas or in the bile ducts. Bacterial infections in various parts of the digestive tube, but especially appendicitis, account for many cases. Congenital anomalies, volvulus, invagination, Meckel's diverticulum, hernia, intestinal angulations and traumatism or wounds occurring during the birth period have also been mentioned, although the last two have been very much doubted.

Most of the cases have been diagnosed postmortem until recent years when, with the aid of the x-ray, early diagnosis has been possible. The author recommends the systematic radiographic investigation of all cases of abdominal distention in the newborn.

Although the exact cause of death in the case here reported was not determined, it seemed most likely to be due to localized circulatory disturbance.

JAMES T. CASE, M.D.

Case of Intersigmoid Hernia with Illustrations of X-Ray Appearances. G. G. Gotlieb. *Brit J Radiol* 19: 429-431, October 1946.

Intersigmoid hernia is a rare condition, only 20 cases having been recorded. It results from the catching of a loop of small bowel in a fossa close to the bifurcation of the iliac artery behind the sigmoid mesocolon. The symptoms are those of acute or chronic intestinal obstruction. One case is reported in which the diagnosis was made by x-ray after a colon injection. The reflux of barium into the ileum demonstrated the point of obstruction.

SYDNEY J. HAWLEY, M.D.

Lymphogranulomatous Strictures of the Rectum. A Resume of Four Hundred and Seventy-Six Cases. Louis T. Wright, W. Adrian Freeman and Joel V. Bolden. *Arch Surg* 53: 499-544, November 1946.

This paper is a study of 476 consecutive cases of fibrous inflammatory (lymphogranulomatous) stricture of the rectum. Lymphogranulomatosis is a virus disease of world wide distribution. This particular manifestation of the condition is more common in Negro women, men with the condition are often perverts. Differences in lymphatic drainage of the genital region in the sexes accounts for this distribution. The most common age is in the fourth decade. The pathogenesis depends on a lymph stasis resulting from the infection, with secondary involvement of the lymph channels by the virus and final scar formation. There is con-

the original—preclinical—roentgenograms of the 5 infants in whom hypertrophic pyloric stenosis subsequently developed differed in no respect from those of the 995 other children. He believes, therefore that it is incorrect to speak of congenital pyloric stenosis. If some slight degree of hypertrophy of the pyloric muscle exists at birth—and thus possibility cannot be altogether excluded—it must be soft, must permit the passage of the peristaltic waves coming from the body of the stomach must have no constricting effect and must not be in a state of permanent contraction or spasm, since it is not evident on roentgen examination.

PAUL W. ROMAN, M.D.

Gastric Carcinoma Incidence and Diagnostic Procedures. Samuel N. Maimon and Walter Lincoln Palmer. *Surg., Gynec. & Obst.* 83: 572-574, November 1946.

The average age of the population is rising and with it also the incidence of cancer. Of the cancer deaths in 1938 approximately 18 per cent were due to cancer of the stomach. The incidence of gastric cancer also rises with age, 76.3 per cent of the authors' series of 566 patients being over 50 years old.

The authors believe there is a trend toward earlier diagnosis as shown by an analysis of 559 cases, of which 47 per cent were diagnosed within six months of the onset of symptoms.

Gastroscopy is of distinct value and with it a correct diagnosis was made in 84.6 per cent of the series here recorded. Repeat examinations are of distinct value, permitting one to more accurately evaluate the changing picture.

The x-ray examination is the most important single diagnostic procedure and by it a correct diagnosis was made in 92 per cent of 533 cases. Determination of resectability by x-ray is unreliable. In a series of cases at the Mayo Clinic 50 per cent of the tumors radiographically believed to be suitable for resection were found unsuitable at operation and 39 others deemed unresectable by x-ray were removed at operation.

ARTHUR W. PRYDE, M.D.

Perforation of a Duodenal Ulcer During Roentgen Examination. J. A. Schilling. *Surgery* 20: 730-743, November 1946.

The reported incidence of perforation of peptic ulcers during or immediately following fluoroscopic examination varies considerably. It is especially high in the European reports which may be due to more vigorous palpation during fluoroscopy. Fifty-seven cases were found in the literature and to these the author adds a further example.

Reaction of the peritoneum to barium sulfate has been investigated by several workers and these studies are briefly reviewed. It has been found that the pylorospasm following experimental perforation of the duodenum causes delay in contamination of the peritoneal surfaces as compared with gastric perforation. Injection of barium sulfate into the peritoneal cavities of rats, as investigated by J. C. Thomas (*J. Path. & Bact.* 43: 285, 1936) resulted in a transient non-specific polymorphonuclear leukocyte migration and large lymphocytic and macrophagic mobilization and later encapsulation with granulation tissue. Most of the particles are phagocytosed by macrophages. Foreign body giant cells are formed in small numbers and only after a relatively long period of time. The

response of the peritoneum in encapsulating every type of foreign body is well known.

The case reported is that of a 72 year-old white male who was undergoing a routine gastro-intestinal examination because of symptoms indicative of gastric or duodenal disease. Some of the symptoms, such as stabbing, burning epigastric pain, most severe around midnight, experienced during the month before admission, suggest the possibility of partial perforation before the examination was begun. The authors do not say whether the duodenal cap was seen before the barium entered the peritoneal cavity, merely stating that "a 250 c.c. suspension was swallowed, containing 200 gm. of barium sulfate. During fluoroscopy, barium was observed to streak out to the right and the left of the duodenal cap and very promptly outlined the right lower boundary of the peritoneal cavity." [Hence it is possible that the perforation existed prior to examination and thus was not due to fluoroscopic manipulation.—J. E. W.] Roentgenograms confirmed the distribution of barium throughout the peritoneal cavity. Operative closure of the duodenal perforation, 1.5 cm. in diameter was immediately carried out. After a stormy course the patient recovered. An eosinophilia reaching 30 per cent, occurred eight weeks postoperatively and lasted for two months. The patient apparently suffered no permanent harm, and was free of ulcer symptoms at the time of the report.

The usual path taken by fluid spilling from a duodenal perforation is described as being first into the subhepatic space and the right infracolic region with concentration low in the right lumbar gutter. The subphrenic spaces are not entered early. The left lumbar gutter and the pelvis are soon involved. In the author's case wide diffusion was observed almost immediately after perforation while fluoroscopy was still in progress. Ten days later, roentgenograms showed the barium in both subphrenic spaces. Adhesions apparently formed quickly as the barium remained in a fixed pattern after the tenth day. None spread to the chest. In experiments with dogs barium was carried along the lymphatics even to the thoracic nodes.

Excellent radiographs of the patient and of the injected dogs and photomicrographs of material obtained from these dogs are included.

J. E. WHITELEATHER, M.D.

Some Problems in Abnormal Intestinal Physiology Associated with Peritoneal Adhesions and Ileus. Ross Golden. *Am. J. Roentgenol.* 56: 555-568, November 1946.

Intestinal obstruction and ileus are two different things. Ileus may follow obstruction—mechanical ileus—or it may occur without obstruction—paralytic ileus.

The distention of the intestine with gas and fluid makes the detection of ileus easy by the roentgen method. The routine procedure is to take films with the patient lying on either side or even erect with the rays directed horizontally to show the fluid levels in addition to a postero-anterior or an anteroposterior projection. Evidence of ileus can be demonstrated earlier by this than by any other method. Distention by gas does not obliterate the mucosal folds of the jejunum which can be seen as fine cross striations in the gas shadow. The mucosal folds of the ileum are obliterated under the same conditions. Thus one may differentiate between gas-distended jejunum and ileum.

showed multiple small opacities in the upper abdomen, 2 to 3 cm anterior to the twelfth dorsal and first lumbar vertebrae. These calcified deposits were irregular in outline and "formed a cast of the entire pancreas." A year and a half later the deposits had increased in number but the diabetic condition showed little change.

A general discussion of pancreatic lithiasis is included. The typical pathognomonic finding in the disease is the demonstration of calcareous deposits in the pancreas. Anteroposterior and lateral views should be made of this region of the abdomen. The stones are usually dense, sharply outlined, multiple, and are grouped on both sides of the vertebral column. In most instances they are confined to an area bounded above by the upper level of the first lumbar or twelfth dorsal vertebra and below by the lower border of the third lumbar vertebra. In the lateral projection they lie 2 to 3 cm anterior to the spine. Gallbladder visualization should be done to exclude gallbladder disease, particularly when the stones are of the multiple-faceted type. Intravenous pyelograms will help to rule out calcification in a horseshoe kidney.

Pancreatic Calculi with Associated Diabetes Mellitus Lee Monroe and Leonard F. Jourdonais J. A. M. A. 132:446-447, Oct 26, 1946

A 46-year-old male, chronically addicted to alcohol, complained of colicky and constant abdominal pain of two days' duration. The pain was of sudden onset, accompanied at the beginning by nausea and vomiting. It radiated to the back in the midline and to the lower part of the abdomen.

Fifteen months earlier the patient had experienced a similar episode lasting three weeks. Gastroscopy and gastro-intestinal studies at that time were negative. The patient was found to have diabetes and was placed on a diabetic regimen, including 30 units of protamine zinc insulin. Within five months he was able to control his diabetes with diet alone and with one minor exception had remained sugar-free till the present illness.

At this time there was tenderness to deep palpation in the epigastrium, slightly to the right of the midline, under this area was a questionable mass. The liver was palpable two fingerbreadths below the right costal margin. Laboratory findings were essentially normal. Cholecystography revealed a normally functioning gallbladder, though a number of small, dense, rounded shadows were visible to the right of the second lumbar vertebra. A gastro-intestinal film showed these to be located entirely within an enlarged C loop of the duodenum, and a diagnosis of true pancreatic calculi was made.

Abdominal pain gradually subsided after five days in the hospital. However, 24 units of 2:1 mixture (regular to protamine) insulin and a diet restricted in carbohydrate were necessary to control the diabetes at the time of discharge.

THE MUSCULOSKELETAL SYSTEM

Disseminated Coccidioidomycosis Localized in Bone
David Sashin, Gregory N. Brown, Norman C. Laffer and Harold C. McDowell. Am. J. M. Sc. 212:565-573 November 1946

In a small percentage of patients having a primary coccidioidomycosis infection, a secondary or disseminated involvement occurs in various parts of the body.

When the bone is involved, the clinical pattern of the disease frequently resembles a tuberculous infection.

A colored male, aged 32, while stationed in Alaska, slipped on the ice and twisted his ankle. A few weeks later he complained of throbbing pain and swelling at the site of the injury. A roentgenogram revealed a destructive process in the lower end of the tibia, with erosion and elevation of the periosteum. Later, draining sinuses developed. Because the patient had spent eleven months in Arizona, a tentative diagnosis of coccidioidomycosis was made. A moderately severe reaction was obtained with the coccidioidin skin test. Biopsy of a large painful femoral lymph node revealed *Coccidioides immitis*. The patient improved following use of a vaccine.

Another colored male, aged 22, complained of pain, swelling, and discharge from the left great toe. A boy had fallen on his foot, and a month later the toe was swollen and three draining sinuses were present. Roentgenograms showed an irregular destruction of the distal phalanx. No pus was encountered at operation. This patient, too, had spent eleven months in Arizona, three years before his present illness. At that time he was hospitalized for an undetermined fever. Coccidioidin skin tests were negative, but complement fixation tests were positive. The sedimentation rate was increased and the patient ran a low-grade fever. The soft tissues about the wound were excised and the wound was curetted. A diagnosis of coccidioidomycosis was returned by the laboratory. This patient later died of disseminated lesions. BENJAMIN COPELAND, M.D.

Present Concept of Osteochondrosis of Growth. Isidoro Pascan. Rev. cubana pediat. 18:412-424, July 1946

The various lesions described by Osgood and Schlatter, by Köhler, by Legg, Calvé, and Perthes, and others, are in some cases characterized by osteochondral ischemic changes at points of growth in full osteogenic activity. The author of this paper believes they should not be called epiphysitis, or apophysitis, or indeed any kind of *itis*, since no inflammatory factor is encountered in these purely aseptic lesions. He prefers the term "osteochondrosis" and completes the designation by adding the bone or region in which the lesion is located, as "osteochondrosis of the capital epiphysis of the femur," "osteochondrosis of the tarsal scaphoid," etc.

After relating the various theories of causation of dyschondroplasia—traumatic, vascular, nervous, congenital, embolic, rachitic or avitaminic—the author concludes that it is the ischemia of the affected region which produces aseptic necrosis of the epiphyseal and apophyseal nuclei. Thus, he believes, is probably the correct explanation for the cause of this affection.

JAMES T. CASE, M.D.

A Roentgenographic Study of "Bends" and "Chokes" at Altitude. W. L. Burkhardt, H. Adler, A. F. Thometz, A. J. Atkinson, and A. C. Ivy. J. Aviation Med. 17:462-477, October 1946

This study was made to ascertain whether x-ray-visible gas might throw some light on the cause of the pain in "bends." Subjects, chiefly 7, who were known to be susceptible to bends were repeatedly exposed to a simulated altitude of 38,000 feet, where a standard exercise using the legs and arms was performed every ten minutes. Four hundred roentgenograms were

siderable variation in the degree of involvement and course, possibly because of variations in the strain of virus and in the host's response.

The stricture is usually cylindric, the length and location are variable. The mucosal surface may be ulcerated, and rectal fissures, condylomata, and perianal fistulae often accompany the disease. Carcinomatous degeneration is sometimes observed. The Frei test is usually but not always positive, hyperproteinemia with reversal of the albumin globulin ratio is the rule. Anemia and amyloidosis are commonly found, but are not specific.

Roentgen study will show the degree and length of the stricture, and is invaluable in high stricture. In low stricture the authors have passed a balloon through the stricture and filled it with sodium iodide solution for contrast, thus avoiding the danger of impaction and complete obstruction. Tuberculosis, ulcerative colitis, carcinoma, diverticulitis, and chemical stricture all possess features of similarity in signs or symptoms and must be excluded. The prognosis is grave, death occurring either as a result of obstruction, complications, or intercurrent disease.

Treatment by drugs, antigens, estrogens, diathermy, and solid carbon dioxide has not been successful in the authors' hands. They have not used radium or roentgen irradiation, but feel that the results obtained in other clinics as observed in patients later seen by them were too poor to justify the procedure. Of the many operative procedures, both major and minor some type of extirpation seems the most effective but the exact operation depends on the condition of the patient and the location of the stricture. Colostomy and the use of sulfonamides are recommended as preliminary measures to control secondary infection. The extensive experience of these authors gives weight to their opinions, and the article will repay a reading in the original.

LEWIS G. JACOBS, M.D.

Cholecystoduodenocolic Membranes. Earle B. Mahoney. *Surgery* 20: 704-717, November 1946.

Many variations in the peritoneal reflections of the upper abdomen have been reported, as might be expected from the embryology of the area. At operation, difficulty may be encountered in differentiating congenital bands from adhesions. Also, associated gallbladder, stomach or duodenal disease may prevent accurate evaluation of the role played by these abnormal peritoneal attachments.

An extension of the normal hepatoduodenal ligament to include the gallbladder, second portion of the duodenum and the hepatic flexure of the colon one of the most common anomalies is known as the cholecystoduodenocolic fold. In this report an attempt is made (1) to illustrate its rarity as a cause of serious symptoms in patients seen at Strong Memorial and Rochester (N.Y.) Municipal Hospitals and (2) to evaluate its role in upper abdominal symptoms.

Various authors have reported "cystocolic folds" in from 15 to 30 per cent of consecutive autopsies. However records of the hospitals mentioned above since their opening in 1926 show only 18 cases in which cholecystoduodenocolic membranes were considered to be the only cause of symptoms proved at laparotomy. In 7 of 100 consecutive cholecystectomies in 1940 congenital bands were found associated with gallbladder disease, although a much larger percentage had inflammatory adhesions. Thus while these bands may be

of fairly frequent occurrence, they cause deranged physiology in only a small proportion of cases.

On the basis of symptoms, the author's 18 cases were of three types (1) those suggesting gallbladder disease, with intermittent attacks of right upper quadrant pain radiating around the costal margin to the back, associated with nausea and vomiting and, in 2 instances with intolerance for fatty foods, (2) those suggesting duodenal ulcer, with epigastric pain exaggerated by eating and frequently relieved by vomiting, but without the periodicity and food relief of duodenal ulcer symptoms, (3) cases with vague upper abdominal pain suggestive of neither gallbladder nor duodenal disease. All the patients had nausea and epigastric distress, none had jaundice or acholic stools. Right upper quadrant or epigastric tenderness was the sole physical sign.

X-ray findings included widening and irregularity of the second portion of the duodenum, localized narrowing of the descending loop of the duodenum with stasis, irregularity of the duodenal cap with pylorospasm, duodenal stasis, fixation together of the gallbladder, hepatic flexure of the colon, and duodenum, angular distortion of the duodenum, large atonic gallbladder with poor emptying, delayed emptying of the stomach, constriction of the colon at the hepatic flexure. Roentgen diagnosis was not possible in all cases. Illustrative roentgenograms are included. Two excellent drawings show the operative appearance.

Of the 18 patients, 13 are considered cured, 3 are improved, and 2 were not helped by operative division of the bands. Those with the most severe symptoms were all cured, those not helped had only vague complaints. Three typical case histories are summarized.

J. E. WHITELEATHER, M.D.

Calcareous Diseases of the Pancreas. Murrell H. Kaplan. *New Orleans M. & S. J.* 99: 203-209, November 1946.

A case of calcareous disease of the pancreas is presented with good illustrations showing the roentgen appearances. A review of the literature follows, in which Snell and Comfort (*Am. J. Digest. Dis.* 8: 237, 1941) are freely quoted. The author repeats the pertinent statement that "the diagnosis of disease of the pancreas would be far more common if the physician would remember that his patient had a pancreas."

SYDNEY F. THOMAS, M.D.

Diffuse Calcification of the Pancreas. Franklin R. Nuzum. *J. A. M. A.* 132: 574-575, Nov. 9, 1946.

A case of diffuse calcification of the pancreas is presented which the author believes brings the total number of recorded cases to 18. The patient, a 23-year-old male, made an uneventful recovery after the removal of the distal two-thirds of the pancreas and diabetes has not developed.

The author believes that it is unlikely that pancreatic calcification is so unusual. It should be considered in the diagnosis when diffuse abdominal pain is present particularly when a history of repeated bouts of pancreatitis is given. A flat plate of the abdomen will establish the diagnosis.

Pancreatic Lithiasis. Edward H. Fischer. *J. Kansas M. Soc.* 47: 455-458, October 1946.

A case of pancreatic lithiasis in a man of 36 with diabetes mellitus is recorded. X-ray examination

in full flexion, stereoscopic views, and occasionally tomography. Sometimes a "close up" is of value, made with a short target film distance, which allows a magnified view with greater detail.

SYDNEY J. HAWLEY, M D

Osteomalacic Dissolution Zones and Obscured Fractures of the Spinous Processes of the Vertebrae Luigi Belloni Schweiz med Wehnschr 76 1107-1109, Oct 26, 1946

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LEWIS G. JACOBS, M D

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Perthes's Disease and Its Occurrence as a Familial Condition. Elizabeth McComas M J Australia 2 584-585 Oct 26 1946

Four cases of aseptic necrosis of the head of the femur are reported in one family, two brothers, a sister, and the four and a half year-old son of one of the brothers being affected. This series of cases is of further interest in that three distinct stages of the disease are represented. The child was seen in a very early stage having had no clinical symptoms when the diagnosis was made, the left femur only was involved but examination of the right femur revealed a certain degree of coxa vara and it is believed possible that a familial tendency to a decreased angle of the femoral neck may be of some significance in these particular cases. The younger of the two brothers, aged twelve, was still in the stage of fragmentation though pronounced flattening of the heads of both femora had already occurred. The other two

patients showed the final picture. In one of these the condition was definitely bilateral, in the other a diagnosis of unilateral disease had been made, but there was some coxa vara on the opposite side as well.

SYDNEY T. THOMAS, M D

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Of a series of 18 patients with dislocation of the acromioclavicular articulation, 14 subsequently showed osseous deposits in the coracoclavicular ligament. This ligament consists of two fasciculi—the conoid and trapezoid ligaments. It anchors the clavicle securely to the coracoid process. It has been likened to a stout cord by which the scapula, and with it the whole upper extremity, is suspended from the outer end of the clavicle.

Dislocations of the acromioclavicular joint are described as incomplete or complete, the latter term being applied when the coracoclavicular ligament is severed. Ossification of the ligament is seen more commonly in dislocation of the complete type. Speed (A Textbook of Fractures and Dislocations, Lea & Febiger, 3d Ed 1935) believes that it results from tearing of the periosteum and the irritation from too early movement and use of the joint.

Anteroposterior roentgenograms of both shoulders in the upright position with a 20 pound weight in each hand will demonstrate widening of the injured joint and elevation of the acromial end of the clavicle. Ossification of the coracoclavicular ligament has been observed as early as twenty-two days following injury. It usually appears as a group of amorphous, cloudy areas of light density below the outer third of the clavicle frequently near the conoid tubercle and usually closer to the clavicle than to the coracoid process. These areas increase rapidly in size and density and within several weeks take on definite characteristics of bone, this being laid down in strands and spicules corresponding more or less to the lines of the fibrous strands of the conoid and trapezoid fasciculi. The bone frequently becomes attached to the clavicle above, but rarely becomes continuous with the coracoid process below. If ossification has not appeared within six weeks, it probably will not occur. The process is not one of calcification but is a true ossification within the ligament. It does not appear to contribute to the disability of the patient. Numerous illustrations of the condition are supplied along with case reports.

CLARENCE E. WEAVER, M D

Congenital Dislocation of the Hip Lorenzo Expósito and Hugo González Rev cubana pediat 18 434-444, July 1946

It is of great importance that early diagnosis of a congenital dislocation of the hip be made. The deformity may easily pass unnoticed in early infancy and make itself evident only when the child commences to stand up and walk. As yet the exact etiology and pathogenesis are unknown.

Congenital dislocation of the hip presents a variety of pathological changes depending on the grade and type of luxation as well as its duration. These changes involve both the head of the femur and cotyloid cavity. When the dislocation occurs toward the iliac bone, the process causes flattening of the femoral head, especially

made of symmetrical joints when one was afflicted with pain (bends). Because the knee was chiefly affected, 280 roentgenograms were made of that joint, including ground control films and films at altitude with and without bends. In most instances in which the knee was involved, both joints were filmed in such a manner as to reveal the growth of gas bubbles and any changes associated with variations in pain.

The presence of pain and gas was approximately equally distributed between the two knees. The pain was not related to the gas found in the joint cavities, bursae, or vaginal sheaths. Extra-articular collections of gas were located as frequently anterior as posterior to the femur and knee joint. Pain occurred as frequently with anterior as with posterior collections, since gas was usually present in both locations. No correlation was found between the amount of gas as measured on the lateral films by a planimeter and pain. Pain was always present, however, when the area of the gas measured exceeded 0.9 sq. in.

In only 22 instances was a roentgen picture characteristic of bends obtained. In these cases a large pocket of gas was present in the popliteal space, extending upward as streaks 5 cm. or longer, apparently dissecting one or more fascial planes.

'Bubbles' almost always occurred from five to fifteen minutes after reaching altitude or after the first or second bout of exercise, and in all but 2 of 13 instances had increased in size when pain occurred. In 15 instances pain was present in a joint when no x-ray detectable gas was present. Partial denitrogenation (30 minutes) appeared to bring about a greater decrease in the incidence of bends than in the amount of gas collected (49 films), though the evidence was inadequate to prove the point.

Two men, exposed 60 and 11 times respectively, had a 'critical focus' in that pain and gas uniformly developed in precisely the same location. In the remaining subjects the occurrence of bends in the presence of x-ray-detectable gas appeared to be a matter of chance.

The authors believe that whether pain is produced by a gas bubble or bubbles depends on the chance location of the bubble at a point in extra-articular tissue where nerves or nerve endings are readily distorted. Chance location does not apply, however, to subjects with a 'proved critical focus' or who manifest the characteristic roentgen picture cited above.

Chest films were made of 3 individuals who had chokes, 27 in the absence and 4 in the presence of symptoms.

Definite enlargement of the maximum transverse diameter of the heart was observed in one man with symptoms of severe chokes.

Sudeck's Atrophy H. A. Sweetapple M. J. Australia 2 581-584 Oct 26 1946

This is a review of the clinical features, etiology and treatment of Sudeck's atrophy with results as gleaned from the literature. No new theories are compounded. Nor are any new features presented except that obviously the author believes that the disease is of reflex nervous origin and involves the sympathetic nervous system.

A Case of Melorheostosis A. David Le Vay Brit J Surg 34 211-212 October 1946

A fourth case of melorheostosis is added to the three previously recorded in the British literature. The con-

dition was an accidental roentgenographic discovery in a boy of nine with mild knock knee. Roentgenograms are reproduced showing involvement of the left ischium, the outer half of the lower femoral epiphysis, both fibular epiphyses, the talus, cuneiforms and the third and fourth metatarsals and phalanges all on the left side.

Radiological Diagnosis of Lumbar Intervertebral Disc Lesions A Report on 160 Cases H. W. Gillespie Brit J Radiol 19 420-428 October 1946

The author of this paper is in agreement with Dandy and others that confirmatory evidence of disk lesions may be obtained in so high a percentage of cases by a study of ordinary spinal films that myelography should be reserved for cases such as spinal tumors. X-ray examination of the spine alone, however, is not sufficient for diagnosis or localization of disk lesions but must be considered in conjunction with the history and physical findings.

The present report concerns 160 cases diagnosed clinically as disk lesions and subsequently verified at operation. In 33 per cent of these the x-ray examinations gave no information to support the clinical diagnosis; the remainder showed pathological findings, some of little help, possibly of an accidental nature, while some—about half of the 160—were strongly indicative of a disk lesion.

The most significant roentgen finding was narrowing of the cartilage space between two vertebral bodies. Forty-one of the cases showed such narrowing between L5 and S1, and in 39 of these (95 per cent) operation showed a prolapsed disk at this point; in the remaining 2 the protrusion was between L4 and L5. Nine cases showed a decreased space between L4 and L5 with operative confirmation in 8 (89 per cent) while in the ninth the protruded disk was between L5 and S1.

The second most significant roentgen sign of disk herniation is localized hypertrophic fringe formation adjacent to the involved disk. Sixteen cases showed hypertrophic fringing between L5 and S1, and in 11 of these (69 per cent) the herniated disk was found at that site, while in the other 5 the protrusion was between L4 and L5. In 12 cases there was fringing between L4 and L5, and in 7 of these (58 per cent) the roentgen localization was confirmed, while in 5 the lesion was between L5 and S1.

The majority of the patients having these two signs were under forty years of age. In older people the signs are not so reliable as they may be the result of simple osteoarthritis, tuberculosis, or spondylitis due to specific organisms such as the typhoid bacillus and staphylococci.

Three other signs may be observed but they are of less significance: congenital anomalies, loss of lumbar lordosis and lumbar scoliosis. These may be coincidental and unless marked should not be regarded as of much importance. The scoliosis may be curved toward or away from the lesion.

Careful technique must be observed in examinations of the lumbosacral spine. First survey anteroposterior and lateral views should be taken. After inspection of these further studies are made as indicated. These consist of lateral views over L4 or L5 depending upon the suspected site of the lesion, a special anteroposterior view of the suspected area with the tube angulated 15 degrees toward the head, right and left oblique views, a lateral view with the patient erect and the spine.

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in its anterior surface, the femoral neck is projected in anteversion, and the angle it forms with the transverse plane tends to become rectilinear. The cotyloid cavity, whose anterior surface is normally smooth and uniform, is roughened by the cartilaginous changes representing the three primitive epiphyseal points which do not complete their development. This widens the cavity, interfering with perfect adaptation with the head of the femur. Furthermore, in place of being directed downward, the cotyloid cavity is directed outward, and the margin is much atrophied, especially in its upper portion, adapting itself more or less to the new position of the femoral head. Thus in the course of time there is formed a false acetabulum.

Attempts have been made to recognize congenital dislocation of the hip radiographically shortly after birth—even before its actual appearance. This potential luxation manifests itself by means of the angle which is formed by the horizontal plane with the plane of the acetabulum. When this angle is greater than 30 degrees the defect should be considered as present (acetabular index of Kleinberg and Lieberman). The affection is more common in the white race and in females. It is usually unilateral. Stress is laid upon the necessity of early diagnosis to prevent invalidism.

JAMES T. CASE, M.D.

Three Cases of Skeletal Changes Round the Knee Joint in Paratyphoid Fever in Infants. Gösta Forssman. *Acta radiol.* 27: 294-299, May 6 1946.

Although bone lesions as a complication of typhoid fever are reported, there are relatively few cases in the literature of bone lesions complicating paratyphoid infection. The author reports three cases in refugee infants from one and a half to four months of age. The clinical courses and roentgen findings were similar and the organism was obtained from the bone lesion in each of the cases. All three patients recovered in from two to three months. Roentgenologically in each case there was a localized destructive process in the metaphysis of the tibia varying from the size of a pea to the size of a coffee berry and surrounded by sclerotic reaction with an associated periostitis and evidence of soft tissue abscess. Roentgenograms are included.

ELIZABETH A. CLARK, M.D.

Arthrodesis of Subtalar and Midtarsal Joints of the Foot. Historical Review, Preoperative Determinations, and Operative Procedure. R. Plato Schwartz. *Surgery* 20: 619-635, November 1946.

The author has made an extensive search of the literature since 1870 for reports relating to correction of deformity and instability of the foot resulting from trauma, infection, disordered nerve impulses, or congenital influences. Arthrodesis is indicated whenever deformity with or without instability is accompanied by a laterally stable astragalus.

The development of the various technics for surgical fixation of one or more of the tarsal joints is traced to the present time. Results vary widely with different surgeons and even with the same operator. A method of preoperative analysis is proposed for more accurately determining the amounts of bone and cartilage to be removed. "Maximum correction of deformity is dependent upon (1) the accuracy of preoperative analysis and (2) the precision with which bone and cartilage are removed at each articulation." Application of the

method is designed to provide a preoperative picture of the best relationship that can be obtained between the bones of the foot.

This concept is expressed in the reconstructed tracing of the preoperative lateral film of the deformed foot. An accurate tracing is made of the mediolateral view. This is cut into three parts and superimposed as shown in the illustrations, on a base line, so as to provide the most desirable relationship of the bones. The overlapping areas then indicate the exact amounts of bone and cartilage which must be removed in each plane of the operation. Superimposition of the preoperative tracing over a postoperative view allows for comparison of the effectiveness of the restoration as planned. Reproductions of the superimposed tracings are not too good, but the principles of the method are quite clear.

Illustrations of the operative procedure are included. A single incision is proposed, extending from the lateral aspect of the navicular, downward and backward lateral to a midpoint of the anterior end of the os calcis thence upwards and backwards just posterior to the fibula ending about 1 inch proximal to the distal end of the fibula.

Results are reported of corrective operations on 45 feet wherein preoperative analysis and the single incision were used as compared with 21 patients in which they were not utilized. The end results in the 45 cases are described as 'uniformly superior'.

J. E. WHITELEATHER, M.D.

GYNECOLOGY AND OBSTETRICS

Superiority of the South African Negro or Bantu as Parturient. O. S. Heyns. *J. Obst. & Gynaec. Brit. Emp.* 53: 405-429, October 1946.

To this study of parturition in African natives the author adds an appendix describing studies made to supplement his previous observations on pelvimetry (*J. Obst. & Gynaec. Brit. Emp.* 52: 148, 1945; *Abst. in Radiology* 46: 306, 1946). Twenty dried Bantu female pelvises for which the true measurements were known were radiographed with the brim horizontal, to determine the accuracy of the method described in the earlier paper. The majority of errors in calculation of the interspinal diameter were less than a millimeter, the mean error being 0.0995 cm. For the brim transverse diameter the average error was -0.589 cm. Calculations of the true conjugate on the other hand showed a mean increase, over the actual measurement, of 0.289 cm. The average calculated brim area was 639 sq cm less than the true planimeter area, the mean percentage of error being -5.67. The calculated area of the cavity exceeded the true area in half the cases and was less than the true area in half the mean error being -1.5 sq cm. Since the conjugate as determined radiographically is on the average about 3.0 mm more and the transverse diameter about 6 mm less than the actual measurements, the calculated brim index will be higher than is really the case.

THE GENITO-URINARY SYSTEM

Has the Cystoscope Maintained Its Revered Position of Former Years? Nathan Blaustein. *Urol. & Cutan. Rev.* 50: 595-604, October 1946.

The author believes that the x-ray examination has assumed a position in the field of urology equal to, if not greater than that of cystoscopy. In this paper he

describes a roentgenologic sign of tuberculosis of the genito-urinary tract which he has designated "incline bladder" and discusses the factors involved in its production. It consists in a "splinting" of the bladder wall on the affected side (whether the lesion is in the kidney, ureter, or bladder, the picture is the same). The musculature is in a high degree of spasm, rigid and unyielding, and instead of the globular roundness seen in the normal bladder there is a sharp flatness beginning at the dome and ending at the base.

A 2.0 or 2.5 per cent solution of sodium iodide is adequate for demonstration of this phenomenon.

Late Effects of Battle Wounds in the Genito-Urinary Tract. Lloyd E. Hawes. *J. Urol.* 56: 561-583, November 1946.

This report on the late roentgenographic changes in the genito-urinary tract from gunshot wounds is based on the personal interpretation of roentgenograms on 40,000 soldier patients and about 3,000 pyelograms from a large Army General Hospital in the United States. All the cases studied were casualties of at least three weeks duration from the European and Pacific theaters and were followed until convalescence. The residual changes on discharge of the patient up to two years after injury are summarized. In most cases other parts of the body were injured simultaneously with the genito-urinary tract.

The changes observed are discussed in separate sections for the kidney, ureter, bladder, and urethra, and representative cases are reported and roentgenographically illustrated. No statistical analysis is attempted. However, a concise outline lists the late roentgenologic changes seen by the author as well as a few other changes reported in the literature. Under *kidney* are listed such main changes as loss of substance, distortion of the drainage system, hydronephrosis and/or pyelonephrosis, retained foreign body, extravasation of dye, calculi formation, calcification of perinephric tissues. Under *ureter* are listed, stricture, fistula to skin and bowel, adhesions, renal stone formation above stricture, and displacement. Under *bladder*, change of shape and position, calculi formation, change in muscle tone due to cord bladder, under *urethra*, stricture, variation in course and caliber, and fistula. Attention is drawn to the fairly frequent occurrence of renal calculi formation unilaterally and bilaterally during prolonged bed rest in orthopedic patients, as well as in other cases, as ureteral structure.

The variety and diversity of the late changes are considerable, and recognition of the types of scarring or deformity of any part of the genito-urinary tract should prove of value. The author feels, in dealing with any discharged soldier presenting himself with a urological problem. However, some of the changes are not associated with symptoms and may confuse the interpretation of abdominal films and pyelograms years after a gunshot wound has healed.

DAVID S. MALBN, M.D.

Wilms' Tumor in a Horseshoe Kidney. E. J. McGinn and J. M. Wickham. *J. Urol.* 56: 520-524, November 1946.

The authors present a case of Wilms' tumor occurring in a horseshoe kidney. A review of the literature revealed only 2 similar cases. Ehason and Stevens (*Ann Surg.* 119: 788, 1944) reported a case of Wilms' tumor arising from the upper pole of the left segment of a

horseshoe kidney, and Rose and Wattenburg (*Urol. & Cutan. Rev.* 49: 305, 1945) described a Wilms' tumor occurring in the isthmus of a horseshoe kidney. Both patients were successfully operated upon.

The present case occurred in a 2-year-old girl. Symptoms were noted two months prior to admission. Treatment consisted of irradiation to a huge tumor occupying the left side of the abdomen, followed by operation. In a three weeks period the patient received a total of 4,000 r equally divided between anterior and posterior fields. Treatments were given daily, one area per day, with 190 kv, 15 ma, 50 cm distance, a 10 x 15 cm port, and 200 r per area. At the completion of the course, there was a marked regression in the size of the tumor.

Operation two months after completion of irradiation revealed a Wilms' tumor in a horseshoe kidney, involving the lower poles of the left and right segments of the kidney and the isthmus as well. The lesion was removed *en masse*, leaving only the superior portion of the right kidney intact. The patient died after discharge from the hospital, presumably from uremia.

The treatment of Wilms' tumor will always evoke controversy among urologists and radiologists. Three points of view are cited. (1) Ladd (*Ladd and White, J. A. M. A.* 117: 1858, 1941) from the Children's Hospital of Boston removed 22 Wilms' tumors in a period of eight years with no operative mortality, in spite of the fact that no preoperative irradiation was given to reduce the size of the tumor. He believes that distant metastases may occur in the three to six weeks interval during which irradiation is administered prior to nephrectomy. About 25 per cent of his patients have survived long enough to be considered cured. (2) Priestley and Schulte of the Mayo Clinic (*J. Urol.* 47: 7, 1942) reported that 39 patients had been operated on for Wilms' tumor in that institution. These had been treated in various ways with respect to irradiation and surgery. Of the entire 39 patients, 6 lived five or more years following surgery, a survival rate of approximately 15 per cent. In the experience of these writers, nephrectomy with preoperative and postoperative irradiation has given the best results. (3) The present authors state that they are accustomed, as noted in the case reported, to use preoperative irradiation and then perform nephrectomy in six to eight weeks. The fact that the tumor occurred in a horseshoe kidney did not alter the management of the case in this instance.

MARLYN W. MILLER, M.D.

Triplicate Ureter. Irvine Smith. *Brit. J. Surg.* 34: 182-185, October 1946.

The author reports a case of triplicate ureter in a child of six months. A cystogram revealed two widely dilated ureters on the left and retrograde pyelography showed a normal right ureter and pelvis. A left nephro-ureterectomy was performed and a third ureter was found arising from the lower pole of the kidney. Since only a single left ureteric orifice was demonstrable cystoscopically, it was assumed that the anomaly was of 'trifid' type, the three components uniting just above or actually in the bladder wall. The three pelves arose separately, one above the other, in the middle plane of the kidney.

The previously recorded cases of triplicate ureter are summarized, and the clinical and embryological significance of the anomaly is briefly considered.

Acute Interstitial Cystitis A Clinical Entity Charles Tahara Carl Lechner and Elmer Hess J Urol 56 535-543, November 1946

The authors describe an acute inflammatory lesion of the bladder wall characterized by the clinical syndrome of urinary frequency, strangury, and hematuria, which they have termed acute interstitial cystitis. The condition appears to result from the inadequate treatment of certain lower urinary tract infections.

Three cases are reported in which the condition followed inadequate penicillin therapy of a urethritis or prostatitis. In one case *Staphylococcus aureus* and a non hemolytic streptococcus were isolated from the urine but no organism was found by routine methods in the other two cases. Grossly the bladder wall, including the muscularis, appears highly inflamed, edematous and hemorrhagic. Biopsy sections showed areas of lymphocytic infiltration, capillary dilatation and hemorrhage. The condition was cured in all cases by large doses of penicillin and arsenical therapy.

The diagnosis can be made from the history and intravenous urography and, therefore it is believed that instrumentation should not be used. The urograms in each case showed a contracted bladder with very small capacity and over-dilatation of the ureters and pelves of the kidneys the picture simulating tuberculosis, cancer, and chronic interstitial cystitis.

JOHN H. FREED, M D

Double and Accessory Urethra George W. Irmisch and Edward N. Cook. Minnesota Med 29 999-1002 October 1946

Two cases of double urethra are recorded. In one an accessory urethra 14 cm in length was shown roentgenographically to end in a blind pouch beneath the symphysis pubis. The accessory canal opened on the surface of the glans penis but did not communicate with the bladder or normal urethra.

The second case was more unusual. Here there was a complete duplication of the urethra associated with other urinary tract anomalies (bilateral duplicated renal calices, pelves, and ureters) as well as a fifth lumbar hemivertebra. The penis was single but gave the appearance of two incompletely formed organs which had fused. The point of fusion of the glans was marked by a cleft on the dorsal and ventral surfaces and each glans had a distinct urinary meatus.

The Proven Ineffectiveness of the Compression Bag in Intravenous Pyelography Hjalmar E. Carlson J Urol 56 609-611 November 1946

The author studied the use of the compression bag as an aid to pyelography in 20 thin young adult males with exertion of as much compression as could be tolerated. The device was found to be of no value in intravenous pyelography. Despite the maximum pressure x rays taken in the erect position showed a rapid emptying of contrast medium from the renal pelvis. Poor pyelograms were obtained in the erect position as compared with those obtained in the dorsal position, the former in most cases defied interpretation. No obstructive properties of a pressure bag on the ureters could be demonstrated.

[Editor's Note: A study of this subject refuting Carlson's conclusions has recently been made by Herbert R. Zatzkin, M D, of the University of Michigan and will appear in a later issue of RADIOLOGY.]

RICHARD C. RIPPLE, M D

THE BLOOD VESSELS

Laminagrams of the Normal Azygos Vein Vinicio Gemignani Radiologia med (Milan) 32 381-389, October 1946

The author, following the studies of Crane, Ottonello, Meldolesi, Lequene, Turano and others, states that postero-anterior roentgenograms will show the normal azygos vein in a large percentage of cases. The portion of the vein which is visible is that which crosses the right bronchus before emptying itself in the superior vena cava. This shadow is enlarged in cases of increased venous pressure due to cardiac decompensation and has been often confused with an enlarged lymph node. Laminagrams will demonstrate the shadow of the azygos vein much more clearly than plain roentgenograms and the author presents a striking example.

CESARE GIANTURCO, M D

TECHNIC

Method for the Evaluation of Calcium Therapy by Roentgenographic Technic. Henry M. Feunblatt and Edgar A. Ferguson, Jr. New York State M J 46 2207-2299 Oct. 15 1946

Calcium supplementation is of importance not only in the treatment of rickets but also to promote good bony growth and the formation of normal teeth in the child. It is frequently used during pregnancy when the calcium demand is increased and is occasionally employed in endocrine and dietary diseases. The measurement of blood calcium levels has not provided an accurate index of the adequacy of calcium supplementation as there has been no constant rise with medication.

By use of Wistar rats and the U. S. Pharmacopoeia XII procedure for the assay of vitamin D, rickets may be produced at will. The authors followed this method and studied the extremities of the rats radiographically. They found that on a calcium-free diet they could demonstrate a constant radiolucent transverse line at the region of the epiphyseal junction even when the animals were receiving a full supply of vitamin D. This occurred within ten days. When calcium was supplied in the amount of at least 0.7 mg per 100 gm body weight at the end of the ten days the films showed normal epiphyseal closure. The results of the tests are in strict conformity with the results of the U. S. P. "line" test for assay of vitamin D and the method has the advantage that the rat is not destroyed so that serial studies may be made. BERNARD S. KALAYJIAN, M D

Notes on an Elastic Radio-Opaque Injection Mass. Ralph Lum, Jr. Anat Rec 96 165-181 October 1946

The formula for a glycerin gelatin lead tetroxide mass which is radiopaque and possesses all the favorable features of latex emulsion without any of its disadvantages has been developed for the arterial injection of human adult and infant cadaver material.

A preliminary survey of the material from 11 adult and 14 infant injected bodies analyzed by stereoscopic x ray films combined with dissection reveals potential value of this medium as a means for studying the epiphyseal vascular patterns in infants and the normal and abnormal gross vascular patterns in muscles, tendons, nerves, bones and joints.

A number of roentgenograms are reproduced.

RADIOTHERAPY

NEOPLASMS

Results Obtained by Contact Radiotherapy Carlos García Rev méd cubana 57 638-657 August 1946
Thirty three tumors of the skin received contact therapy with different filters varying from no filtration to 2.5 mm Al. At the same time 2 cases were treated at 200 kv. Nineteen cases were healed. The remainder had to receive complementary irradiation at 120 kv and 200 kv. The author believes from a practical point of view that the same results could have been obtained by a low voltage unit supplied with cones of different shapes, without greatly lengthening the time of treatment.
JAMES T. CASE, M.D.

Roentgen Therapy of Pituitary Adenomas Simcun T. Cantril and Franz Buschke, Editors, Radiation Therapy Conference West J Surg 54 403-407 October 1946

While roentgen therapy is accepted as the primary procedure of choice in pituitary adenomas it is still necessary in each case to determine the respective indications for irradiation and surgery. Irradiation has the advantage of no mortality and more permanent arrest of the tumor growth in successfully treated cases. It is futile however, in the presence of a cystic tumor (and approximately 20 per cent of all pituitary tumors in due time become cystic). Also the progress of decompression following irradiation is much slower than after operation and this may be important if there is danger of blindness. In some instances there may even be an increase of pressure due to reactive edema of tumor tissue requiring surgical intervention. Treatment of pituitary tumors thus demands close co-operation between the neurosurgeon and radiation therapist. Failure of radiation therapy may be due to cystic degeneration of the tumor, incorrect diagnosis or inadequate treatment.

The authors have treated 10 cases by radiation since 1939. Seven of the tumors were of the chromophobe type and 3 of the eosinophilic type. All of the patients with chromophobe tumors had associated visual disturbances prior to therapy. Two of the 7 cases have been treated too recently for evaluation. Of the other 5 patients 3 are well with normal eye grounds or stationary field defects four years twenty-one and eight months respectively, following therapy. Two died with advanced cystic lesions. The 3 patients with eosinophilic adenomas are all well—2 of them seven years and 1 nineteen months following therapy. In one case normal menstruation recurred following irradiation.
MAURICE D. SACHS, M.D.

Further Experience with Radiotherapy in Cancer of the Corpus of the Uterus J. Heyman and Sven Benner Acta radiol 27 328-333 May 6 1946
The method of treatment of carcinoma of the corpus of the uterus since 1934 at the Radiumhemmet has been packing the uterine cavity with radium applicators. Surgical procedures have been done only after primary radiological treatment has failed. Of the 316 patients so treated 205 or 64.9 per cent were alive and free from evidence of carcinoma after five years. Of the 354 patients treated by other methods prior to 1934 45 per cent were alive and free from evidence of neoplasm after

five years. Further analysis shows that 17 per cent of the cured patients in the early group required operations, while in only 10.7 per cent of the group treated by packing was hysterectomy necessary. Details of the method of packing and of the type of applicators are presented.
ELIZABETH A. CLARK, M.D.

NON-NEOPLASTIC DISEASE

Rhinoscleroma Observations Based on a Study of Two Hundred Cases Esteban Reyes Arch Dermat & Syph 54 531-537 November 1946

Rhinoscleroma is a disease involving the skin and mucous membrane of the nose, mouth, pharynx and larynx. It causes a thickening and overgrowth which makes the countenance of the patient resemble that of a rhinoceros or hippopotamus. The disease occurs in both sexes and is somewhat more common in women. It is apparently not transmitted and is not hereditary. It usually occurs between twenty and forty years of age and runs a course of from eight to twenty years. Poor hygiene may be a factor. The disease may be divided into three stages. In the first or rhinitis period the symptoms are those of acute coryza. There is a fetid nasal secretion and rhinoscopic examination reveals a reddened mucous membrane and a beginning hypertrophy of the nasal septum. In the second stage the coryza symptoms disappear and a thickening of the nasal septum lips and pharynx occurs. Wavy or reddish infiltrations appear around the nostrils. Later the larynx becomes thickened, causing a change or loss of voice. In the third stage the rhinoscleroma pushes the nose upward and laterally causing monstrous deformities. Thenose may be completely obstructed. Tumor formations appear on the palate, further involvement of the larynx makes breathing difficult.

Rhinoscleroma has been treated by all sorts of drugs none of which affects its course. Attempts at extripation and curettage only cause the infection to advance with greater rapidity. The only therapeutic agents which the author has found of avail are roentgen rays and azosulfamide. Roentgen therapy is given in doses of 200 r per day for seven consecutive days with the following factors: 200 kv 0.5 mm Cu and 1.0 mm Al filtration and 50 cm focal skin distance. Five series of treatments per year are given for two years in the first and second stages of the disease. In the third stage the prognosis for complete healing is reserved, but the author has succeeded in keeping his patients in good condition able to work and live a routine normal life.
JOSEPH T. DANZER, M.D.

Radium Therapy in Aerotitis Media Page Northington U.S. Nav. M. Bull. 46 1559-1567 October 1946
The author reports a series of 60 cases of aerotitis media in aviators treated by means of the radium applicator (50 mg). Audiometric tests were done at some time after the acute stage of aerotitis media had subsided and repeated four weeks following the last radium treatment. Better ventilation of the ears had changes in atmospheric pressure was obtained in the 90 per cent of the patients that received adequate treatment and were followed up and usually there was improvement in hearing acuity if the defect had been

recently acquired The technic for using the applicator is described

Roentgen Treatment of Bursitis of the Shoulder
Barton R Young Am J Roentgenol 56 626-630, November 1946

Eighty-seven patients with bursitis of the shoulder were treated with roentgen therapy Sixteen cases were acute (symptoms present one week or less) 23 were subacute (symptoms from one week up to two months), and 48 were classed as chronic (symptoms longer than two months) Fifty six of the 87 patients were females The presence of calcium in the soft tissues of the shoulder is of less importance than the history and clinical findings in the diagnosis of bursitis In the subacute and chronic forms it is important to rule out the many other causes of chronic shoulder pain

The physical factors employed for therapy were 180 kv, 8 ma, 0.5 mm Cu plus 1.0 mm Al filter, and 50 cm target skin distance. The usual individual dose was 150 r (in air) Acute cases received from one to three daily doses with an additional dose after one week if necessary Many of the subacute cases received two treatments per week for a total of four treatments Chronic cases were treated the same way or were given four treatments at weekly intervals

All but two of the patients with acute bursitis were relieved of pain, and the response to treatment was prompt More than two thirds of the subacute group reported complete relief in two weeks or less, and only a few were not benefited In only one third of the group with chronic symptoms was a good result obtained and almost 50 per cent reported no relief of pain Favorable results are not dependent on the disappearance of calcium deposits The results with recurrent bursitis are comparable to those obtained in patients with initial attacks
CLARENCE D WEAVER M D

Disseminate Lupus Erythematosus Unsuccessfully Treated with Penicillin, Roentgen-Ray Castration and Serum Albumin John B Johnson and Edward C Mazique Ann Int Med 25 859-862 November 1946

Because of a report by Rose and Pillsbury (Ann Int Med 21 1022, 1944) suggesting a possible relationship between ovarian function and lupus erythematosus, the present authors employed roentgen castration in addition to other measures in a case of disseminated lupus erythematosus coming under their care. Treatment was unsuccessful and the patient a Negro woman of thirty-two years died after an illness of approximately ten months

A Pharmacological and Radiological Study of Hemophilia Marcus Ostro and David I Macht South M J 39 860-867, November 1946

This article is a study of the action of x rays on blood coagulation *in vitro* and *in vivo* in experimental animals and in two human beings with hemophilia *In vitro* irradiation of blood samples from both normal animals and the two hemophilic subjects definitely shortened the clotting time as compared with normal non-irradiated controls obtained at the same time. It was also evident that the best thromboplastic effects are gleaned after exposure to x-rays passing through a composite filter equivalent to 2 mm of copper This effect *in vitro* is best produced with dosages ranging from 63 to 105 r Larger doses do not lead to greater diminution in clotting and may actually be less effective. The

same thromboplastic effect of x-ray was obtained by exposing the animal itself and also the human subjects to small doses of deeply penetrating x rays These findings justified a cautious and controlled study of x ray treatment in the two hemophilic subjects and it was found that in each instance, coagulation of blood samples *in vitro* was accelerated and what is more interesting clinically a shortening of clotting time was observed for some days after exposure. The dosage in treating these patients was usually 63 r given over the spleen on three different dates two days apart One treatment was given from the anterior aspect of the spleen a second directed laterally, and a third posteriorly

As regards the systemic reactions of the two subjects Mr A, who was in normal health except for his hemophilia, curiously enough suffered from roentgen sickness after each treatment Mr B, on the other hand who was certainly in poorer health had no particular reaction The total amount of radiation received by Mr A in a period of eighteen days was 378 r following which his health was excellent In the case of Mr B the total amount of x-ray energy received over a period of 30 days was 693 r after which as he himself expressed it he was feeling much better than for a long time before

The present report is of course, a preliminary one and is given here in order to call attention to a new approach to the treatment of hemophilia, a condition for which there has hitherto been no remedy Since the publication of the paper the authors have treated 5 other hemophilic patients with x-ray as described and in each case there has been a marked shortening of the coagulation time lasting for at least several days

HUGH O'NEILL M D

TECHNIC

X-Ray Therapy with a Continuously Rotating Beam. Part I. Apparatus and Associated Physical Problems. R. J Munson Brit J Radiol 19 405-419, October 1946

A logical extension of cross firing with multiple beams is to have the beam rotate continuously about an axis passing through the lesion This may be accomplished by rotating the patient with the beam stationary or moving the tube about a horizontal axis with the patient stationary The latter is preferred by the author as immobilization and theoretical distribution of the radiation may be obtained with greater accuracy

The apparatus and method of setting up the patient are described, and calculations for depth isodose curves for varying conditions are given in detail As these cannot be adequately summarized in an abstract, a study of the original article is advised

The author demonstrates clearly that a more efficient distribution of depth dose with relation to skin dose and integral dose may be obtained by rotation For example in a patient with an anteroposterior thickness of 20 cm being treated for carcinoma of the esophagus with 6 stationary beams 10×4 cm a tumor dose of 6000 r will correspond to a maximum skin dose of 5800 r and an integral dose of 23 Mgr With a rotating beam moving through 90 degrees and a 10×3 cm port, a tumor dose of 6000 r will correspond to a maximum skin dose of 3500 r and an integral dose of 18 Mgr If the beam rotates through a complete circle 360 degrees the integral dose may be larger because of increased absorption where the depth of the tumor from the surface is greater This increase may be important when

the integral dose is already equal to the maximum recommended value, and in these circumstances it would be better to arrange that the tube should rotate through one or more arcs of limited angular width and in such positions that the mean depth of the tumor is as small as possible

With the beam rotating through an arc, the distribution is also influenced by the relation between the angular speed and the direction. Theoretically therefore it should be possible to secure a wide variety of distributions by changing the displacement time relationship. It is also possible to alter the distribution by centering the beam away from the axis of rotation, say at the edge of a tumor, which in some situations might give a more desirable distribution. The physical problems presented by this arrangement are formidable, but are now being worked upon.

SYDNEY J. HAWLEY, M.D.

Points Regarding the "Time Factor" in Roentgen Irradiation with Divided Dosage Hugo Ahlbom *Acta radiol* 27 223-227, May 6, 1946

Attention is called to the recently published book by Strandqvist (reviewed in *Radiology* 46 526, 1946) in which the cumulative effects of roentgen therapy and dosage fractionation were carefully studied in 280 cases of carcinoma of the face and lip. The results of treatment were plotted in respect to total dosage and duration of treatment, and an iso-effect curve was obtained. Those cases in which severe reactions or late necrosis occurred and which therefore must have received an overdosage are found almost entirely above the curve, while most of the cases with recurrences fall below the

curve. The optimum zone for therapy has the general shape of a parabola in the usual co-ordinate system.

Reasoning from the curve thus obtained, certain practical applications are pointed out.

1 The incomplete cumulative effect of irradiation is illustrated, $t \propto$, the cumulative effect is less marked with treatment of short duration than with treatment of long total duration.

2 The value of protraction in treatment of long duration is questioned because the iso-effect curve rises so slowly as the time factor increases, and particularly when fractionation is carried through two or more weeks.

3 It is suggested that treatment should be completed before severe erythema has developed, because of the increase in radiosensitivity of skin in a state of acute roentgen erythema. ELIZABETH A. CLARK, M.D.

An Instrument for Calculating Roentgen Ray Doses from Condenser Chamber Readings Sven Benner *Acta radiol* 27 243-247, May 6, 1946

An instrument has been devised by means of logarithmic scales and a triple setting mechanism to simplify dosage measurement from condenser chamber readings.

The equation $D = kd \times \frac{760}{b} \times \frac{273 + t}{293}$ is solved. D is

the roentgen dose, k is a constant for each condenser chamber under standard conditions, d is the loss of potential observed, b and t are the atmospheric pressure and temperature, respectively, of the chamber during irradiation. The instrument is described in detail and diagrams are included. ELIZABETH A. CLARK, M.D.

EFFECTS OF IRRADIATION

The Connexion Between Roentgen Ray Risks for Workers and Changes in Their Blood Pictures Matts Helde. *Acta radiol* 27 308-315, May 6, 1946

The Swedish Roentgen Ray Protection Law of 1941 attempts to protect patients, personnel working with roentgen equipment, and others who may receive exposure. The law requires periodic inspection of offices and equipment and annual blood counts of personnel. The author presents a preliminary report on the findings. From the survey of more than 2,000 offices tables for the risk-indexes were set up and the offices were classified and subdivided into four groups according to the factor for amount of exposure. When abnormalities in the blood studies were plotted against the four major risk groups, the correlation was found to be significant. It is also pointed out that anemia and leukocytopenia are injuries rather than premonitory changes while hypersegmentation, granulocytopenia, pathologic lymphocytes and shift to the left are early changes and are important in indicating undue exposure.

ELIZABETH A. CLARK, M.D.

Importance of Sulfydryl in the Treatment of Corneal and X-Ray Burns Archie E. Cruthrds. *Am J Surg* 72 500-509, October 1946

Five years' experience with the treatment of 500 cases of x-ray and corneal burns by the use of sulfydryl is reported. The burns were mainly facial, particularly in and about the eye. The author gives a concise review of previous experimental and clinical studies and relates

these works to his own experiences. Function of the agent is related to the nutrition and/or oxidation effects in traumatized areas of skin.

The material used was an aqueous solution in strengths of 1:20 or 1:40, with triple-distilled water as the vehicle. This was applied as a spray, continuous soaks, or drops. Ointment of similar strengths has also been beneficial.

Of particular interest to radiologists are the reports on three specific cases.

(1) X-ray burn between the inner canthus of the eye and nose, following therapy for skin carcinoma. The burn was described as being so severe that "surgery was considered." Rapid favorable response with total healing resulted after use of sulfydryl.

(2) Spreading ulcer on the thigh, part of an x-ray burn extending from the inguinal region to the heel. Marked healing was obtained.

(3) An ulcerated burn on a radiologist's hand. Five years later the treated site was still completely healed in every way.

This reparative agent is non-toxic and to all intents and purposes non-irritating. Visible attributes are the following:

(1) Scarring is prohibited or greatly reduced. (2) Infection is prevented or eradication of existing inflammation hastened. (3) Rapid epithelial growth occurs and smoothly covers injured areas.

The results noted in the author's report are enthusiastic yet reservedly summarized. He urges further

clinical and experimental studies to arrive at a clearer understanding of underlying reasons for the beneficial effects so far found
JOSEPH P. TOMSULA, M.D.

Use of Radon Ointment in the Treatment of Late Irradiation Ulcers David Kursh, J. Francis Mahoney, and Eugene P. Pendergrass. *Am. J. M. Sc.* 212: 395-403, October 1946

Until recently radiation ulcers have proved notoriously refractory to medical treatment. Uhlmann in 1930, first began to use radon ointment, and has since demonstrated its therapeutic value (see *Radiology* 38: 445, 1942). The ointment, which is made by dissolving radon under pressure in linolin, contains a very small amount of radioactive material. Ninety per cent of the radiation is composed of alpha particles, which are absorbed in the most superficial layers of the tissue. It is believed that capillary proliferation is stimulated in the ordinarily avascular bed of the ulcer.

When late radiation ulcers are seen, a biopsy may be necessary to determine the presence of malignant change. Even a prompt response to radon ointment does not exclude such a possibility.

Necrotic tissue, which will act as a barrier to the alpha particles, should be removed with zinc peroxide or sulfanilamide-allantoin ointment for several days. The ulcer should be cleansed, debrided, and dried so that the application may be made as close as possible to viable tissue. The ointment is applied with a wooden tongue blade to a thickness of about 1 mm, evenly over the lesion, including a normal tissue margin. One cubic centimeter should suffice for 10 sq. cm. of a lesion. An airtight dressing, consisting of rubber dam, oil silk, or cellophane, is applied over the ointment. After a specified time, the patient removes the dressing, and after a superficial cleansing, applies a bland ointment or a bactericidal preparation.

The ointment is obtainable commercially in strengths of 100, 200, 500, and 1,000 electrostatic units per cubic centimeter. These correspond to the commercial alpha-particles 40, 80, 200, and 400 m.e. per c.c. The concentrations are also graded—mild, moderate, strong, and special. The authors have used the 200 e.s.u. (moderate) ointment applied for eight hours once a week. Occasionally applications have been made twice a week. The treatment extended from four to twelve weeks.

One of the most striking features was the prompt relief of pain when the treatment was combined with methods for the control of the concomitant infection. An early response usually progressed to rapid and complete recovery. In some cases, however, persistence in treatment over a long time was required for complete healing. Meticulous control of infection, eradication of slough, and cleansing and dressing of a wound may yield gratifying results in what appears to be a hopeless situation.
BENJAMIN COLEMAN, M.D.

Response of Tradescantia Pollen Grains to Radiation at Different Dosage-Rates P. C. Koller. *Brit. J. Radiol.* 19: 393-404, October 1946

Pollen grains of *Tradescantia* (spiderwort) were irradiated with x-rays at rates of 50, 5, 0.5, and

0.25 r/min, and with gamma rays at 5, 0.5, 0.25, and 0.1 r/min. The total dose in each instance was 200 r. The number of chromosome and chromatid breaks was counted in random samples of 20 metaphases out of 80 to 100 nuclei, usually from anthers of the same flower bud, and fixed at twenty-four, forty-eight, and seventy-two hours after irradiation.

The most sensitive stage in the life cycle of the cell was found to be between twenty and thirty hours before metaphase and to correspond to the time of chromosome reduplication. There was considerable individual variation in the counts of cells fixed at twenty-four hours, presumably because the cells and chromosomes were in the most susceptible condition when the radiation was given and fixation took place. More consistent counts were found at forty-eight and seventy-two hours.

There was no evidence to show any difference in frequency of breaks after irradiation by roentgen or gamma rays at the same dosage rate. The average number of breaks was less in samples fixed at seventy-two hours after irradiation at 0.5 r/min, and for those fixed at forty-eight and seventy-two hours after 0.25 r/min. At low dosage rates, not only were the number of breaks less, but there was a smaller number of interchanges of fragments. This suggests that at lower intensities some recovery takes place. With the lowest dosage rates, 0.1 r/min of gamma rays and 0.5 and 0.25 r/min of x-rays, cell division was not suppressed.

Differences in environmental and developmental conditions can affect the frequency of breaks. These experiments were performed during two growing seasons, 1944 and 1945. There was significant difference in the rates in the two years, although the other conditions of the experiment were the same.

These observations suggest that the amount of damage to chromosomes depends to a great extent on the relation of the length of the life cycle of the cell to the duration of irradiation.

SYDNEY J. HAWLEY, M.D.

Effect of Extra Vitamin B Feeding on Rats Exposed to Weak Gamma Radiation. G. M. Scott. *Brit. J. Radiol.* 19: 329-332, August 1946

Rats were exposed to gamma radiation in doses varying from approximately 60 to 85 r per week for a period of four months. Studies were made on the effect on weight gain and fertility with and without feeding extra vitamin B.

Rats receiving extra vitamin B showed greater weight gain than the controls, and their coats were in better condition. Rats receiving radiation but no extra vitamin gained less than the controls.

Both female and male irradiated rats were mated with unirradiated. The irradiated females became pregnant as often as normal, but there were many cases of abortion; some died in parturition, and few of the litters were reared. These effects were not as pronounced in the rats receiving extra vitamin B. No offspring resulted from matings with irradiated male rats.

SYDNEY J. HAWLEY, M.D.

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Diagnosis and Treatment of Carcinoma of the Uterine Cervix A Panel Discussion¹

EDWIN C ERNST, M D, Chairman

A N ARNESON, M D, WALTER J SIEBERT, M D, JOHN I BREWER, M D, HARRY H BOWING, M D,
GEORGE W WATERMAN, M D, J A DEL REGATO, M D, E L JENKINSON, M D

Introduction

EDWIN C ERNST, M D

St Louis, Mo

I HOPE THAT WE MAY have an interesting discussion and present without too many words the facts relating to cancer of the cervix, based on the observations of my confreres, who are experienced in certain special lines of radiation and surgical therapy. These gentlemen have assumed a grave responsibility, since they will be subject to attack by you and by the individual members of the panel.

First of all, I should like to introduce the various essayists. Dr Arneson will discuss the clinical diagnosis of cancer of the cervix, and Dr Siebert will discuss the pathology, Dr Brewer will take up the

surgical phases and Dr Bowing the radium treatment, Dr Waterman will present his experiences with interstitial radium therapy, and Dr del Regato will speak on transvaginal roentgen irradiation. Last but not least, my friend, Dr Jenkinson, is going to present some statistics which should throw further light upon this important subject.

These essayists will present their positions briefly, stating the salient points, following which each of them may address such questions as he desires to the others. Finally, the audience will have an opportunity for questions and discussion.

I am very happy to present to you Dr Arneson of St Louis

¹ Presented at the Thirty second Annual Meeting of the Radiological Society of North America, Chicago, Ill Dec 1-6, 1946

Clinical Diagnosis of Carcinoma of the Cervix

A N ARNESON, MD¹

BIOPSY IS THE basis for diagnosis in cancer of the cervix. Histologic examination does not, however, present all the necessary criteria for establishing prognosis and selecting suitable methods of treatment. Prognosis depends largely upon the clinical stage which the cancer has reached. It is obvious, of course, that we cannot expect success in every favorable case, nor should we expect failure in all advanced lesions. There are other factors which affect the response to treatment.

A high degree of radiosensitivity does not imply a high degree of curability. In markedly sensitive lesions there may be rapid regression with prompt recurrence and a short span of life, while tumors slow to regress may sometimes permit survival for longer periods. Such variations in clinical behavior will be reflected in survival rates. One might expect a degree of correlation to be found between the microscopic appearance of tumors and their curability. There is, indeed, an established relationship between anaplasia and favorable degrees of radiosensitivity, but it is difficult to correlate histologic characteristics with clinical results.

We may, then, expect variation in response to treatment not accurately predictable upon the basis of the clinical stage of advance or the histologic appearance of the biopsy specimen. In some instances regression will be prompt and complete. In others resistance to radiation will be equal to or greater than that of the adjacent normal tissues. Some patients will show a slow but incomplete regression, with persistent cancer that remains clinically inactive for long periods. Such differences in clinical behavior must be due to variations in the biologic properties of tumor growth.

Further evidence of differences in bio-

logic behavior can be found in comparing the gross characteristics of different tumors. There is no definite relationship, for example, between the size of the primary lesion and the stage of clinical advance. Large bulky tumors may be confined to the cervix itself, on the other hand, extensive infiltrations and even distant metastases can occur with but slight enlargement of the cervix. Neither is there any definite relationship between the duration of symptoms and the extent of involvement. Patients with early lesions may have had symptoms of cancer for relatively long periods, while others with more advanced tumors may have sought treatment immediately after the first suggestive sign. Variations in the size of the primary lesion and in duration of symptoms can be explained upon the basis of the infiltrating qualities of tumor growth. A tendency toward outward proliferation or toward deeper infiltration forms a basis for classification into different biologic types. In the attempt to classify lesions into everting and infiltrating types, however, we come immediately upon the problem of disposing of a third form, which shows a crater and is not easily fitted into one of the basic varieties. The cratered forms present, in addition, the factor of infection, which is always present to a considerable degree due to their extensive ulceration. The presence of severe infection has a definitely unfavorable effect upon tumor regression.

(1) *Everting types* produce a cauliflower-like growth that begins as a small raised lesion which can grow rapidly to a size that practically fills the vagina. They vary in their infiltrating qualities, but even the larger forms may present clinical evidence that the disease is limited to the cervix itself. Because of a minimum of

¹ From The Edward Mallinckrodt Institute of Radiology and the Department of Obstetrics and Gynecology, Washington University School of Medicine, and the Barnard Free Skin and Cancer Hospital, St. Louis, Mo.

connective tissue they are soft and friable. They bleed easily and profusely, due not only to their friability but also to their copious blood supply. For these reasons, bleeding and a thin watery discharge tend to appear early in the disease. Everting cancers present a favorable prognosis. They are, as a rule, radiosensitive and, because of their early symptomatology, are usually diagnosed in a favorable stage of clinical advance.

(2) *Infiltrating types* produce diffuse enlargement of the cervix, which usually proceeds slowly despite the fact that deeper tissues are invaded. The cervix becomes hard and nodular and may become indistinguishable, with obliteration of the vaginal fornices. The tumor frequently grows beneath an intact mucous membrane. Ulcerations are few in number and tend to occur late in the disease. Bleeding is not an early symptom but may be preceded for a fairly long period by a thin watery discharge. Infiltrating types are characterized by a maximum of fibroblastic activity and a scant blood supply. A possible explanation of these qualities can be made on the basis of an attempt on the part of the normal tissues of the host to resist invasion by throwing up a barrier of connective tissue, with an associated decrease in vascularity. In this group prognosis is poor, due to resistance to radiation and to the fact that the disease has usually advanced to an unfavorable stage by the time diagnosis is established.

(3) *Cratered lesions* may be assumed to have begun as one or the other of the above types. Formation of a crater is due to loss of tissue from slough following necrosis. Death of tissue can occur spontaneously in tumors inadequately supplied with blood but is more often the result of infection. There is greater risk of severe infection in the everting types, due to their friability with frequent ulceration. Further evidence of the association between cratered forms and everting types can often be observed in the rather favorable degree of radiosensitivity of the latter despite the infection usually present.

To classify cancers of the cervix into different groups according to the gross characteristics of the lesion is of more than theoretical importance. Prognosis can be established more accurately if biologic qualities are considered in conjunction with stage of clinical advance and histologic appearance of the biopsy specimen, and an estimation of prognosis is of value in selecting suitable methods of treatment. The selection should be more effective, however, if made upon the basis of tumor response to be expected. This is not intended to imply that lesser amounts of radiation can be employed in the more radiosensitive lesions. It does hold that a given quantity of radiation will produce greater biologic change in certain tumors.

For a panel discussion of this kind, certain points seem worthy of mention in the discussion of clinical diagnosis. Among the everting lesions the prospects are favorable for rapid and complete regression. In such cases radiation given at a relatively high intensity may be tolerated fairly well by normal tissues of the tumor bed and produce favorable results. Treatment at lower intensities is, however, a more practical procedure. Infiltrative tumors will be more radioresistant. Regression will proceed slowly, and the fibrosis and ischemia already present in the tumor bed may result in untoward damage to its structures. Destruction of the tumor bed by radiation can permit unrestrained growth of cancer, due to removal of all the normal inhibitory mechanisms. In the treatment of infiltrating types, therefore, a low intensity of irradiation is essential. If the course of roentgen therapy is protracted or the radium dosage is divided among several applications, the total time of irradiation can be extended for administering greater total doses over the longer period of slow regression. The use of intravaginal x-ray therapy may prove to be of greater value in this group than in the everting types.

Cratered forms present a special problem due to the high degree of infection usually present. This may result in increased

radioresistance The action of radiation is essentially traumatic Infection also produces tissue trauma In an infected environment, the tumor cells may develop resistance to certain forms of trauma Infection also lowers the threshold to necrosis An amount of radiation believed practical for a clean lesion may, in the presence of infection, result in an extensive breakdown of tissue The problem is, therefore, similar to that found in the infiltrating type of cervical cancer A plan of low-intensity irradiation protracted over a long period is more effective than large doses applied over a shorter time Since many cratered forms are derived from everted lesions, however, the degree of radiosensitivity may be improved with decrease in infection

Finally, mention should be made of the value of the classification here discussed in relation to the use of surgery in the treatment of cervical cancer Among indications given for radical hysterectomy is the avoidance of persistent radiation ulcers and reappearance of cancer in the cervix itself Risk of those sequelae is greatest in the infiltrating types Due to delayed bleeding in such patients, however, the disease is often advanced beyond an operable stage by the time diagnosis is established There may be evidence in the form of a thin watery discharge for long periods before bleeding occurs That symptom is worthy of greater attention in programs of cancer control

4952 Maryland Ave
St Louis 8 Mo

Dr Ernst Thank you Dr Arneson

I am very happy to have Dr Siebert with us He is a pathologist and is particularly interested, as I know you are, in the diagnosis of early or questionable cancer Following Dr Siebert, Dr Brewer, who is a clinician as well as a laboratory worker, will present the surgical aspects of cancer of the cervix

Pathologic Aspects of Carcinoma of the Cervix Uteri

WALTER J. SIEBERT, M.D.

St. Louis, Mo

CANCER OF THE uterus is the most frequent cancer in the female, and approximately 90 per cent of the cases are primary in the cervix, while only about 10 per cent are primary in the corpus.

The frequency of uterine cancer must be referred partly to the anatomical and physiological characteristics of the organ, more especially to its exposure to various forms of trauma and irritation. Endocrine factors and age probably also play a role. Multiple pregnancies with their attendant repeated lacerations disturb the normal structure and functions of the cervix, interfere with its nutrition, and expose it to chronic irritation and inflammation. A chronic cervicitis precedes cancer in approximately 75 per cent of cases. The routine examination of such tissue frequently reveals abnormalities in the morphology and position of the epithelium which constitute a precancerous condition.

Thus the prophylaxis of cancer of the cervix is a problem largely connected with prevention of lacerations and the proper post-partum care of the cervix, especially in women who have had multiple pregnancies and have reached their fortieth year. Periodic examinations, preferably with adequate biopsy material rather than vaginal smears, are to be emphasized.

Another important group of women who develop cancer of the cervix are those who have had a supravaginal hysterectomy, since an average of 1 to 3 per cent of supravaginal hysterectomies, without removal of the cervix, are followed by cancer. It is my opinion, based on these figures, that panhysterectomy is justified in all cases where hysterectomy is indicated.

The prognosis of cancer of the cervix depends upon its early recognition and the histologic grade of the neoplasm. Shields, Warren and others have classified tumors of the cervix according to their origin from

the various layers of the normal squamous covering of the vaginal portion of the uterus. Tumors arising from the upper portion they designate as spinal-cell carcinoma, those that arise from the transitional cells of the deeper layers as transitional-cell carcinoma, and those having their origin in the basal or germinal layer as the fat spindle-cell type. The tumors may be further divided according to Broders' classification, based on the degree of differentiation of the cells, into Grades I, II, III, and IV, in that order of malignancy.

According to Warren's studies, only about 4 per cent of the spinal-cell carcinomas were found to have metastasized to the lymph nodes, of the fat spindle-cell carcinomas, on the other hand, 87 per cent had lymph node metastases. Thus, though tumors of the latter group are more radiosensitive, they are more rapidly invasive and their prognosis is accordingly unfavorable.

In choosing an area from which to take a biopsy specimen, a Schiller test is useful. I prefer to be present when a biopsy is done in order that I may see from what part of the tumor the tissue is taken and be certain that it is adequate in amount. I insist, also, on personally supervising the imbedding of the tissue in order to make sure that the suspicious area noted clinically appears in the sections. In all cases where a suspicious lesion or one suggestive of early carcinoma is present, serial sections should be obtained, as single sections have often proved negative in cases in which serial sections of the same lesions revealed early carcinoma.

[EDITOR'S NOTE: This paper, as presented, was illustrated by a large number of lantern slides, showing the various clinical stages and histologic types of cervical carcinoma.]

3 Oakleigh Lane
Ladue, Mo

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already present at operation, I do not believe we can tell from the clinical aspect when a lesion is absolutely *in situ* or early

I am glad that Dr Siebert brought up the serial section procedure. This brings out another point in favor of surgery. If we are to make an early diagnosis, we must have tissue to examine. Surgery removes those tissues and gives them to us for examination. If those that are taken out are thoroughly and completely studied, our knowledge of carcinoma of the cervix may be increased. Therefore, those who do surgery should study the specimens.

Indications for surgery as recommended by Meigs and others are as follows. Surgery should be done only in Stage I or II (League of Nations' classification). Surgery should be used only as an adjunct to irradiation. Surgery should be limited to patients under fifty and in good physical condition, with no contra-indication of any type to operation. Also, the patient must be thin (and this is most important). There must be no lower vaginal metastases. I would add here that under no conditions do I subscribe to removal by simple amputation of the cervix of any lesion which is either suspicious or definitely diagnosed as carcinoma. This is to be condemned. If the patient has a suspicious lesion, or an early intraepi-

thelial carcinoma, there is but one surgical procedure to be used—a Wertheim or modified Wertheim operation, removing the complete uterus, the broad ligament tissues, and adnexa. With this method five-year cures can be anticipated—but only anticipated, since it will take another ten or fifteen years before figures can be accumulated.

The primary complication to surgery, as recorded recently, is the occurrence of fistulas. This complication must be accepted if we are going to do surgery. To operate, one must acquire technic and that takes time. In Meigs' first 50 cases the incidence of ureterovaginal fistula was 8 per cent, but in his next series there was none.

Those surgeons who are technically qualified, those surgeons who will pathologically study their material, and those surgeons who will have adequate follow-up in large numbers should make a study of this problem for us, so that in five, ten, fifteen, or twenty years we shall have a true evaluation of the use of surgery under new conditions in the treatment of carcinoma of the cervix. A general swing toward surgery for carcinoma of the cervix should not be made at this time.

104 S Michigan Blvd
Chicago 3, Ill

*Dr Ernst: Thank you Dr Siebert and Dr Brewer.
We will now have the subject of intracavitary radium therapy presented by Dr Bowing.*

Carcinoma of the Cervix Surgical Aspects

JOHN I. BREWER, M.D.

Chicago, Ill.

I BELIEVE THAT WE should take a very sane view of the surgical treatment of carcinoma of the cervix. Fundamentally I am a surgeon, and fundamentally I like it. The time, however, has come when we can realize that a discussion such as this means simply that there is no wholly adequate treatment of cervical carcinoma. If there were, we would need no discussion.

Surgery was condemned in the past, and rightfully so. Primary mortality was high. Bonney's figure of 10 per cent over his lifetime (and he represents the master so far as certain operative procedures are concerned) are beyond the limits to which we could subscribe. With the advent of therapeutic agents—transfusion, penicillin, sulfa drugs, etc—it could be expected that primary operative mortality would be reduced. Since we think that all forms of treatment have failed, fundamentally, to cure carcinoma, we are permitted, I believe, to search further for better methods. Further search reveals, however, that so far there is nothing in the way of new types of treatment to present, so it is feasible again to try surgery.

The present goal of the surgeons is earlier diagnosis of cervical cancer so that operation can be tried. If they do nothing other than to make it a conscious process of everyone to look for early carcinoma, their program may be called a success.

Surgical treatment of cancer of the cervix is limited to Stages I and II, and rightfully so, but to get cases in Stage I or II (League of Nations' classification) one must, of necessity, search for them, and those of us who want to treat them surgically and thus acquire statistics and make them available as rapidly as possible, must immediately begin a detailed search for early cases.

Dr. Siebert has seen some early cases,

but not nearly so many as he should. Indeed, no pathologist has seen as many as he should. But that is not the fault of the pathologist. It is the fault of the clinician—the fault of us who do not take enough biopsies and do not search diligently enough for carcinoma.

Patients are now doing their part more adequately, as demonstrated by studies that have been made. While it was formerly eleven months from the onset of symptoms before the patient presented herself for treatment, that time has now been shortened to five months, but many patients, after they present themselves, do not get, immediately enough, surgical therapy or radiation therapy. The diagnosis is not made.

The reason we feel that surgery should be used on a limited number of patients is, first, that cures—or preferably five- or ten-year arrest of the disease—with radiation have not been adequate, second, that the primary operative mortality is now reduced. It should be no higher than 15 per cent in competent hands. Another point is that we, in our experience, have seen too many local recurrences of carcinoma in the cervix itself, or in the upper vaginal vault, following x-ray or radium therapy. Removal of the cervix by surgery obviates a recurrence there and, since we also remove the upper portion of the vagina, carcinoma cannot recur at that site. In addition, surgery removes the lymph nodes of the pelvis. These nodes may be involved by carcinoma. Just how many are thus involved is hard to discern, since most patients have had some irradiation prior to surgery. It has been shown that lymph node metastases may be present even in early or so-called early carcinoma of the cervix—in *situ* cancer, or Stage I of the League of Nations' classification. Since such metastases may be

therapist in his treatment of the lesion. All procedures are carried out with a minimum of trauma.

In some cases, the cervical canal is eccentric to the main malignant tumor. In that event, the applicator is placed in the center of the malignant medullary mass. In cases in which the mass is very firm, a slight stab wound may have to be made for the applicator.

As a rule, no anatomic difficulties are encountered in cases in which the lesions are classified as Stage I or II. The applications of radium may be carried out daily so long as no distressing systemic effects occur. However, lesions which are classified as Stage III or IV may distort the anatomic landmarks and make their identification tedious and in some cases impossible at the first treatment. A large medullary cervical mass or a large crater with necrotic walls is the chief offender in this regard, but as time passes, these features of the malignant process are resolved, the field is restored to a more normal state, and radium can be applied throughout the involved region. Distribution of the radium is an essential element in the intensive broken-dose method. Although the individual response to treatment will vary, it can, at least in a measure, be anticipated.

Judgment and skill are necessary for the greatest individualization of the intracavitary method of treatment. The response should be a rather slow one instead of a rapid change, which may result in necrosis and distressing complications, as a persistent discharge, foul odor, hemorrhage and fistulas. Judgment is essential in selecting and outlining the type of radium treatment at the time of the first consultation. The treatment should be designed for cure or palliation, though, to be sure, the total treatment time may furnish data that will alter the first estimation. In that event, the alteration should be fully discussed with the staff and, if accepted, should be charged against the judgment of the radium therapist. Provided all zones can be treated as out-

lined, the procedure is classified as a complete treatment (1) designed for cure, otherwise, it is classified as a limited treatment designed for palliation. On subsequent visits, the complete radium treatment should not be repeated, however, limited radium treatments may be applied to sites of active involvement in order to extend the period of palliation.

Supplemental Roentgen Therapy Roentgen therapy is started a few days before radium therapy is completed. The pelvis is divided into two anterior and two posterior fields (2). The roentgen rays are generated at 200 kv² and are filtered with approximately 0.75 mm Cu and 1.0 mm Al. A dose of 500 to 700 r is applied to each field. In selected cases, the doses are divided, and 250 to 350 r are administered daily. For very obese patients, additional filtration is used to obtain better penetration of the rays, but the dose per field is about the same as that employed in the average case. The doses are measured in air. In the average case in which the lesion is classified as Stage III, a second course of roentgen therapy is usually given after an interval of three months. We do not use larger doses of roentgen rays because they are likely to cause irritation of the bladder or intestine. The irritation of the intestine may cause bleeding from the mucous membrane and eventually may produce scarring and obstruction.

Roentgen therapy was employed alone in 41 of a series of 1,491 cases in which irradiation therapy was used in the years 1915-29, inclusive (1). In cases in which roentgen therapy is employed without radium therapy, the roentgenologic technic is the same as that which has been described, with the exception that the doses applied to each field may be increased to approximately 1,000 r.

RESULTS

The early response to treatment is most gratifying. The first response observed is the control of bleeding, which

² Prior to 1923 we used roentgen rays generated at 135 kv.

Intracavitary Radium Therapy for Carcinoma of the Uterine Cervix¹

HARRY H. BOWING, M.D.

IN THE MAIN, intracavitary radium therapy may be defined as the application of radium to the surface of a lesion occurring in any hollow place or space. Not only is it the oldest form of radium therapy of carcinoma of the uterine cervix but it also is a conservative method. Many improvements and refinements have made it most effective. Our experience with this method at the Mayo Clinic covers a period of thirty years. During that time, the technic employed has been rather constant, which permits the widest possible interpretation of the variable factors inherent in the patient and the disease.

The history, bimanual palpation, inspection and sounding of the genital tract, especially in the predominating Stage III lesion, are essential for diagnosis and treatment. A general physical examination and the required laboratory tests, including removal of tissue from the primary lesion for microscopic study, are absolutely essential from the standpoint of good management. A knowledge of pathology and physiology will sharpen the interest of the therapeutic radiologist. As a rule, constant vigilance by the physician and patient will be an important element in obtaining a good immediate and late result.

The standard platinum tube containing 50 mg. of radium sulfate (element) is used, the walls of the tube are 1 mm. thick. The applicator may contain one or more tubes. When distance is employed, it is maintained with 2 mm. or 1 cm. of Para rubber. The following factors are approximate for treatment of the average Stage III lesion. The time of the application may vary from three to twenty-four hours, the dose, therefore, ranges from 300 to 2,400 milligram hours. The interval between applications is one to seven days. The total time consumed may be ten to

twenty-one days. The treatment area is divided into zones, and the dose in milligram hours applied to each zone is as follows: to the vaginal zone 2,100, to the proximal cervical zone 1,400, to the distal cervical zone 1,400, and to the intra-uterine zone 2,000 to 2,400.

The method requires hospitalization only for the day of the treatment. The time that the patient has to spend in the hospital is from eight to ten days. No general anesthetic is used. A dose of 1/6 grain (0.01 gm.) of morphine sulfate may be administered hypodermically before the treatment. Barbiturates are used sparingly. All other drugs are given by the physician on the medical hospital service. In the past few years, the field has been dusted with a sulfonamide drug at the same time that radium therapy is applied. All applications of radium are made with the patient in the knee chest position. With gentle unilateral separation of the labia, air is admitted to the vagina, which permits a type of endoscopic examination. The endoscope consists of a Sims' speculum and a direct electric lamp with a suitable handle. The vagina becomes a distended hollow organ and permits (a) visual and palpatory examination of the normal and pathologic tissues, (b) selection of the site for the removal of representative material for biopsy, (c) the location of anatomic landmarks, (d) the placement of the radium applicator, (e) the placement of gauze packing to hold the applicator in position and to obtain as much distance as possible between the applicator and the adjacent normal anatomic structures. As treatment proceeds, the gross changes occurring in the neoplastic tissue owing to the rays of radium are readily visualized and their distribution and intensity guide the radium

¹ From the Section on Therapeutic Radiology, Mayo Clinic, Rochester, Minn.

52.9 per cent, lived three or more years after the completion of treatment, of 739 traced patients who received a limited course of radium therapy, only 158, or 21.4 per cent, lived for three or more years (3)

COMMENT

Evidently therapeutic radiologic judgment is an important element in prognosis, since it may possibly increase the chance of survival for three years or more. All supplemental efforts should be employed to further the possibility of applying a *complete* course of treatment. However, as a word of caution, we must not overtreat a very advanced lesion and in this way bring about distressing features to add to the difficulties of an already overburdened and apparently seriously ill patient. No data are available for an estimation of the morbidity rate in this series of cases. Morbidity occurred, however, but we were not impressed by the number and severity of the reactions.

Today the responsibility of the therapeutic radiologist in the treatment of carcinoma of the uterine cervix is great. The patient and her possible restoration to health should be his major concern. The outline of a plan of radiation treatment made at the initial consultation and designed for cure or palliation and to meet the therapeutic requirements of the patient will produce the best results.

The radium technic must be very flexible. For example, it must be adaptable to the therapeutic requirements of Stage I and Stage II lesions, notwithstanding the fact that they are few in number when compared with those of Stage III and Stage IV, as well as to the recurring and modified lesions and their usual distressing complications. The radiologist's comprehension and knowledge will guide him in the selection of the most effective treatment factors.

There is no substitute for patience and an allotted time in determining the most effective therapeutic strategy. Interest in the patient's recovery must extend

through the initial period of treatment and the months and years that follow. With judicious, skillfully applied intracavitary radium therapy as the initial treatment, supplemented by roentgen therapy, it is possible to influence favorably the discharge, odor, pain, bleeding, and such potential distressing sequelae as fistulas, unilateral edema of the extremities, and hydronephrosis. In some cases, sound permanent healing of the primary lesion will occur in a minimal treatment time with a low mortality and morbidity rate. There should be no conflict between radium therapy and roentgen therapy, I contend they should be employed to complement each other, the greater the co-operation and co-ordination of effort the more effective will be the treatment.

There are few data in the therapeutic radiologist's field of endeavor that will furnish material for generalization, instead, the patient and the disease are both characteristically individual, as well as the response to treatment. However, in a measure, a certain pattern of satisfactory response will be observed, though this cannot be definitely predicted.

With an enlightened womanhood, an alert physician, and a skillful specialist guided by sound therapeutic judgment, the initial result should be prompt and the late result should be more permanent, or the period of palliation should be longer and more enduring.

SUMMARY

Briefly stated, the intracavitary, intensive broken-dose method of radium treatment, followed by supplemental roentgen therapy, furnishes a wide range of individualization for the greatest number of patients who have carcinoma of the uterine cervix. The treatments can be designed for cure or palliation. The immediate subjective and objective response occurs rather promptly. As time has passed, favorable statistical data have become available to support our initial interest and to encourage us to improve and refine

may occur in two or more days. The distressing unilateral aching in the back, hips, and legs may be relieved in four or five days. The discharge and odor of the lesion are the last features to respond to treatment.

The patients are instructed to return for examination every three or four months during the first year after irradiation treatment, every six or nine months during the second and third years, and every year thereafter.

The following analysis of the results of treatment is based on 1,491 cases in which this type of treatment was employed at the Clinic in the years 1915 to 1929, inclusive (3). As previously stated, in 41 of these cases roentgen therapy was the only type of treatment employed. Fifteen, or approximately 1 per cent of the patients died while they were in the hospital.

As the patients returned during the first year after their treatment, the late response was found to be equally gratifying. The uterine and adnexal infiltration was markedly reduced in extent. In some cases, the pelvic structures were free of any palpable characteristic infiltration due to residual malignant activity. As the years passed, statistical data were available to confirm our initial clinical impressions. During the first five years of our experience with this type of treatment, that is, in the years 1915 to 1919, inclusive (4) the treatment was used in 288 cases. Follow-up data were obtained in 264 of these. Of the 264 traced patients, 38, or 14.4 per cent were living three or more years after the completion of treatment. During the years 1920 to 1924, inclusive, the treatment was used in 556 cases, follow-up data being obtained in 522. Of the 522 traced patients, 185, or 35.4 per cent, were living three or more years after the completion of treatment. During the years 1925 to 1929, inclusive, the treatment was used in 647 cases. Follow-up data were obtained in 585 of these cases, and of the 585 traced patients, 250, or 42.7 per cent, were living three or more years after the completion of treatment. In several cases

in each of these groups, the lesions had been modified by treatment before the patients came to the clinic.

This rather definite increase in the percentage of patients living three or more years after the completion of treatment was due to several factors, including (a) a satisfactory method of vaginal endoscopy to facilitate the placement of the applicator and gauze packing with minimal trauma, (b) the observation of the vaginal field during the initial days of therapy to guide the selection of the most effective treatment factors for each patient, (c) better distribution of the radium applicators in the vaginal and uterine fields of involvement, (d) the early recognition and treatment of potential and actual complications, such as bleeding and serious hemorrhage, localized inflammation, and necrosis of tissue.

In 1,079 of the 1,491 cases, the disease had not been modified by previous treatment. In these cases the lesions were classified as follows: Stage I, 13 cases; Stage II, 85 cases; Stage III, 825 cases; Stage IV, 156 cases. Follow-up data were obtained in all of the cases in which the lesion was classified as Stage I. Nine, or 69.2 per cent, of the 13 patients were living five or more years after the completion of treatment. Follow-up data were obtained in 78 of the 85 cases in which the lesion was classified as Stage II. Of the traced patients, 47, or 60.2 per cent, were living five or more years after the completion of treatment. Follow-up data were obtained in 753 of the 825 cases in which the lesion was classified as Stage III. Of the 753 patients, 224, or 29.7 per cent, were living five or more years after the completion of treatment. Follow-up data were obtained in 138 of the 156 cases in which the lesion was classified as Stage IV. Of the 138 traced patients, 9, or 6.5 per cent, were living five or more years after the completion of treatment.

The type of radium therapy employed has a definite effect on the prognosis. Of 565 traced patients who received a complete course of radium therapy, 299, or

Interstitial Radium Therapy in Carcinoma of the Cervix

GEORGE W. WATERMAN, M.D.

Providence, R. I.

RADIUM IN THE FORM of long element needles of low intensity, 2 to 3 mm platinum filtration, with a long time interval, has been in use for the treatment of cervical carcinoma at the Rhode Island Hospital since 1926, a period of almost twenty-one years. Prior to 1926, small steel needles of 5 mg. content were used for this purpose. In 1926, on a visit to London, Dr. H. C. Pitts saw some use of these longer needles and brought home the idea. We undertook an experiment to see what could be done with interstitial radiation of this type, and we have had no reason to regret our decision. The great advantage lies in the fact that radium in this form can be placed out into the pelvic tissues, the zone where carcinoma is invading.

In our use of these needles, we have no idea at any time of pushing them out into empty space. We seek the edge of the growth, as we can feel it by way of the vagina and rectum, making a careful examination, under good light in the operating room, with the patient relaxed under an anesthetic. We then slip the needles into the advancing zone of growth.

The needles are element needles, they have the same intensity when we take them out as when we put them in. They are of small content, the radium is evenly distributed throughout their length, 0.66 mg. per c.c. of active length, and the filtration is such that only the gamma rays are effective. It is our belief that no other type of needle will exactly fit this purpose.

In addition to the parametrial needles, we have a platinum capsule of 20 mg. content that will deliver into the cervico-uterine canal approximately 3,300 mg. hours over a period of seven days. All this radium is implanted and is left in place for the full time—168 hours. We think that protracted treatment of this

type—small doses given over a long time interval—is a very important factor, both in causing the disappearance of the cancer cells and in preserving and perhaps fortifying the condition of the surrounding tissues.

The second great advantage that we find in this method of therapy is its extreme flexibility and adaptability to all types and conditions of cancer of the cervix. It does not make any difference whether the vagina is a short and narrow one, cone-shaped in the upper third, or whether it is a broad one, with a large cauliflower growth. The radium needles are easily inserted, perhaps with the finger in the rectum to guide them carefully into the uterosacral ligaments or into the part of the pelvis which is being invaded.

Another advantage is the non-necessity of using large sources of radium against the vaginal walls in order to obtain a relatively small amount of radiation in the deeper tissues, with consequent reduction in vaginal breakdown and slough. Also, the fact that only 50 or 60 mg. of radium is all that is needed to treat a case represents some advantage to smaller institutions. The entire radium treatment is given in one dose.

The disadvantages of excessive incidence of sepsis, fistula formation, and intestinal injury, which have caused so many gynecologists and radiologists to fear interstitial radiation, have not been apparent in our experience. We have had our troubles with all these complications; it is true, but not in excess of such complications reported by others using different methods.

With the use of deep x-ray therapy in infected cases, preliminary to radium, and with the sulfa drugs and penicillin, it would seem that fear of infection from interstitial sources is no longer a valid objection, in fact, we have had no immediate mor-

this conservative method of radium treatment for carcinoma of the uterine cervix

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Mayo Clinic
Rochester, Minn

*Dr Ernst Thank you Dr Bowling
The next presentation will be some pointed remarks along the line of
interstitial radium therapy by Dr Waterman, from Rhode Island*

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Providence, R. I.

RADIUM IN THE FORM of long element needles of low intensity, 2 to 3 mm platinum filtration, with a long time interval, has been in use for the treatment of cervical carcinoma at the Rhode Island Hospital since 1926, a period of almost twenty-one years. Prior to 1926, small steel needles of 5 mg. content were used for this purpose. In 1926, on a visit to London, Dr. H. C. Pitts saw some use of these longer needles and brought home the idea. We undertook an experiment to see what could be done with interstitial radiation of this type, and we have had no reason to regret our decision. The great advantage lies in the fact that radium in this form can be placed out into the pelvic tissues, the zone where carcinoma is invading.

In our use of these needles, we have no idea at any time of pushing them out into empty space. We seek the edge of the growth, as we can feel it by way of the vagina and rectum, making a careful examination, under good light in the operating room, with the patient relaxed under an anesthetic. We then slip the needles into the advancing zone of growth.

The needles are element needles, they have the same intensity when we take them out as when we put them in. They are of small content, the radium is evenly distributed throughout their length, 0.66 mg. per cc. of active length, and the filtration is such that only the gamma rays are effective. It is our belief that no other type of needle will exactly fit this purpose.

In addition to the parametrial needles, we have a platinum capsule of 20 mg. content that will deliver into the cervico-uterine canal approximately 3,300 mg. hours over a period of seven days. All this radium is implanted and is left in place for the full time—168 hours. We think that protracted treatment of this

type—small doses given over a long time interval—is a very important factor, both in causing the disappearance of the cancer cells and in preserving and perhaps fortifying the condition of the surrounding tissues.

The second great advantage that we find in this method of therapy is its extreme flexibility and adaptability to all types and conditions of cancer of the cervix. It does not make any difference whether the vagina is a short and narrow one, cone-shaped in the upper third, or whether it is a broad one, with a large cauliflower growth. The radium needles are easily inserted, perhaps with the finger in the rectum to guide them carefully into the uterosacral ligaments or into the part of the pelvis which is being invaded.

Another advantage is the non-necessity of using large sources of radium against the vaginal walls in order to obtain a relatively small amount of radiation in the deeper tissues, with consequent reduction in vaginal breakdown and slough. Also, the fact that only 50 or 60 mg. of radium is all that is needed to treat a case represents some advantage to smaller institutions. The entire radium treatment is given in one dose.

The disadvantages of excessive incidence of sepsis, fistula formation, and intestinal injury, which have caused so many gynecologists and radiologists to fear interstitial radiation, have not been apparent in our experience. We have had our troubles with all these complications; it is true, but not in excess of such complications reported by others using different methods.

With the use of deep x-ray therapy in infected cases, preliminary to radium, and with the sulfa drugs and penicillin, it would seem that fear of infection from interstitial sources is no longer a valid objection, in fact, we have had no immediate mor-

tality in 326 consecutive cases up to January 1946. In the Spring of 1946, we had one death from a pulmonary embolus on the second day after the radium was removed.

The results obtained, as measured by five-year survivals, have been excellent and have shown consistent improvement. In the last 198 cases the five-year survival rate (absolute) was 38.9 per cent, for 171 cases treated with radium, the figure (relative) was 44.4 per cent.

The needle we use is a long, delicate instrument, having a trocar point that is blunted. The radium is distributed evenly throughout the active length, and insertion can be done with practically no trauma. We do not fear the puncturing of large vessels or of the ureter. We do not feel that, if one of the needles came to lie across the ureter in any one spot, it would have any terrifically bad effect. In fact, our urinary complications have been slight, very few in number. If the point of the needle sticks out into the peritoneal cavity, we are not particularly worried. There is no radium in the point, and it is dull. It will do little harm. We are very careful

and, by putting a finger in the rectum when inserting the needles posteriorly, we believe that we can largely avoid perforation of the peritoneum.

The method of applying the radium in a fairly early case may be described. With the finger in the vault, the needles are inserted almost under direct palpation and are distributed around the cervix. To insert the posterior needles, the finger is placed in the rectum and sterile drapes are placed over the perineum, the vagina is retracted by a Sims' speculum, the point of the needle is placed, and the needle is then directed into the uterosacral ligaments or toward the sides, or kept within the confines of the uterus posteriorly. A large gauze pack keeps the needles in place and serves to retract the vaginal walls.

[EDITOR'S NOTE. At this point a number of slides were presented, showing the method of introducing the radium needles and their distribution in the cervix. The illustrations from which these slides were made appear in a paper by Waterman, Dr Leone and Tracy. *Am J Roentgenol* 57: 671, 1947.]

155 Thayer St
Providence 6 R. I.

*Dr Ernst: Thank you, Dr Waterman.
We shall now continue with a discussion of roentgen therapy by the
transvaginal method. Dr del Regato.*

Transvaginal Roentgen Therapy in Carcinoma of the Cervix¹

J A DEL REGATO, M D

Columbia, Mo

IN TALKING OF THE relative merits of transvaginal roentgen therapy in carcinoma of the uterine cervix, I would like to insist first upon the fact that whatever the means of internal treatment and the technic of its administration, whether this is intracavitary or interstitial radium therapy or transvaginal roentgen therapy, it constitutes only a complement of the external irradiation. In the majority of cases treated, the results will depend mostly upon the adequacy of the external irradiation, which logically should have preceded the internal phase of the treatment.

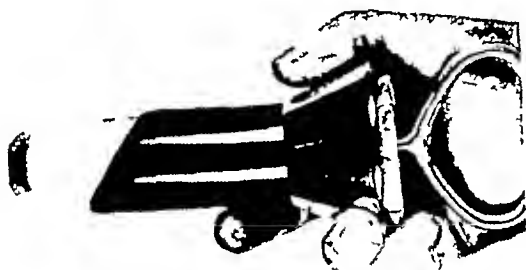


Fig 1 Author's vaginal speculum with a metal head, a transparent shaft, and a plunger to facilitate introduction

Allen, Caldwell, Pusey, and many among the pioneers of radiation therapy tried transvaginal roentgen therapy. Their sporadic attempts never crystallized. The late Edwin A. Merritt is to be credited for having revived this form of treatment and for eloquently and forcibly pointing out its possibilities in the treatment of carcinoma of the cervix.

Merritt used the Ferguson bakelite specula after he had tried to use the walls of a urine specimen bottle as a speculum. Erskine devised an ingenious speculum made of expanding metal blades. This speculum is very applicable in early cases,

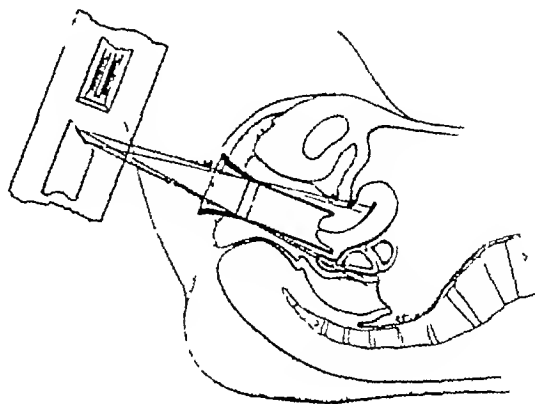


Fig 2 Irradiation through a transparent-wall speculum allows the field to open to about 6 cm in diameter at the level of the cervix

but when the walls of the vagina are invaded, the use of an expanding speculum is not practicable. Wasson and other workers have preferred metal cylinders for the exclusive or even segmental irradiation of the cervix; this method may also be satisfactory in early cases, but I am convinced that it leads to serious inaccuracies. While collaborating with Merritt, I introduced a speculum composed of a metal head for the protection of the vulva and of a shaft transparent to radiations (Fig 1). In its present form, this speculum allows a wide irradiation of the cervix, fornices, and adjacent parts of the parametria, while protecting, when required, the bladder and rectum (Fig 2). In practice, a set of specula of several lengths and widths is necessary.

In our hospital we have now treated with transvaginal roentgen therapy following external irradiation, over 200 consecutive cases of carcinoma of the cervix of all stages. Not a patient has been refused treatment, none has received radium, and

¹ From the Department of Radiotherapy, The Ellis Fischel State Cancer Hospital, Columbia, Mo

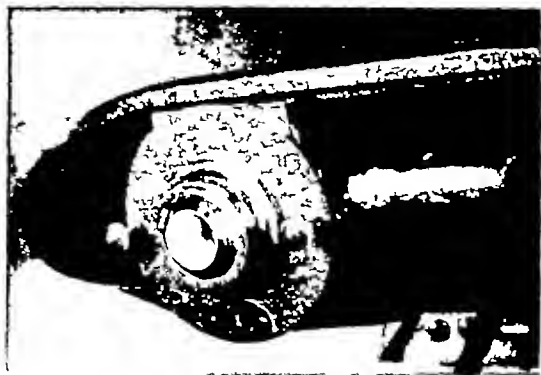


Fig 3 A tube head piece, fitting into the vaginal speculum, to maintain it in place during treatment

very few have not completed treatment. Of 52 primary cases that applied for treatment in our hospital in 1943, only 2 failed to receive complete treatment. The patient is placed in the lithotomy position with the legs comfortably supported. The table is tilted to allow the intestine to fall out of the pelvis. The widest and longest speculum which can be introduced is used. The speculum head is adaptable to a corresponding part in the tube-head (Fig 3). We prefer radiations of moderate penetration, such as obtained from 140 to 150 kv equipment, but also prefer to filter as heavily as possible, usually through 0.5 mm of copper. The target-cervix distance is 25 cm. It is preferable to administer the treatment within two weeks, before the appearance of vaginal radioepithelitis. A very large total dose is not necessary when an adequate external irradiation has preceded. We administer a total of from 3,000 to 4,000 roentgens (measured in air at the level of the cervix) in from ten to twelve days.

Transvaginal roentgen therapy has secured a definite place in the treatment of carcinoma of the cervix. It has the advantage of completing the external ir-

radiation without trauma to the healing tissues, without infectious complications, which so often hamper the practice of intracavitary curietherapy. Transvaginal roentgen therapy assures a more homogeneous irradiation of the cervix and adjacent structures, it requires no anesthesia or hospitalization, it can be sufficiently protracted to reduce to a minimum the untoward effects of irradiation. Even when the bladder or rectum is invaded, a vesicovaginal or rectovaginal fistula seldom occurs, due to the slow effect, which allows retraction of the tissues and vaginal atresia, thus avoiding the fistula formation. It is our impression that there is a lesser number of local recurrences when transvaginal roentgen therapy is used and that failures are mostly due to parametrial recurrences, these should be ascribed to the lack of penetration of our external irradiation.

I would have liked to quote five year survival rates of my own, but I do not have these figures at present. I have just recapitulated the results in 52 consecutive, unselected patients with carcinoma of the cervix who applied for treatment to our hospital in the year 1943, having had no previous treatment. All but 2 patients received external roentgen therapy, followed by transvaginal roentgen therapy, no radium was used. The results now—after a minimum follow-up of three years—are as follows: 26 patients have died of cancer and 4 others have died of intercurrent diseases without evidence of recurrence, 22 patients are alive and without evidence of cancer, or a 42 per cent three-year survival. We need not emphasize that there is no pretense of comparing these figures with five-year control statistics.

Ellis Fischel State Cancer Hospital
Columbia Mo

*Dr Ernst Thank you Dr del Regato
We shall now conclude with some statistical remarks by Dr Jenkinson*

Five-Year End-Results in the Treatment of Carcinoma of the Uterine Cervix

E L JENKINSON, M.D., E L PIRKEY, M.D., and F J HAMERNIK, M.D.

Chicago, Ill

OUR PURPOSE is to outline the five-year end-results of an unselected series of 98 cases of squamous-cell carcinoma of the uterine cervix treated in the period 1935-41, inclusive. Mention will also be made of the various technics employed down to the present writing. Cases which were treated prior to 1935 are not included, as there is no accurate means of determining the precise dosage.

TABLE I CASES TREATED
(Period 1935-41 Inclusive)

	Treated	Followed	Not Followed	Follow-up
Stage I	16	9	7	56 2%
Stage II	13	8	5	61 5%
Stage III	33	30	3	90 9%
Stage IV	36	28	8	80 0%
TOTAL	98	75	23	76 5%

TABLE II RESULTS IN ALL STAGES

	Followed	Died of Cancer	Died of Other Causes	Five Year Survival	Known Survival to Date	Not Followed Beyond Five Years
Stage I	9	2		7(77%)	5	2
Stage II	8	1		7(87 5%)	7	
Stage III	30	25		8(26 6%)	5	
Stage IV	28	27		1(3 5%)	1	
TOTAL	75	55(73%)		23(30 6%)	18(24%)	2(3%)
Stages I and II	17	3		14(82 3%)	12(70 5%)	2(11 7%)

The 98 cases reported are unselected and comprise the usual cases seen in the radiological department of a civilian general hospital located in a large city. They represent all walks of life, being about equally divided between charity and private patients. The follow-up is 76 5 per cent of all cases, that is, 75 cases were followed from the beginning of radiation therapy for at least five years or until death. It should be noted that the relatively low percentage of follow-up probably stems directly from the war-time social upheaval of the period 1941-46.

Schmitz' clinical classification was used throughout in order to correlate the extent of the disease when first seen with the result. Of the 75 patients followed, 55 or 73 per cent are known to be dead, 18 or 24 per cent are still alive, 23 or 30 6 per cent were alive and free of disease after at least five years. There are one ten-year

cure, 2 nine-year cures, 2 eight-year cures, 4 seven-year cures, 5 six-year cures, and 9 five-year cures.

TABLE III YEARS SURVIVAL

Years survival →	5	6	7	8	9	10
Stage I	2	2	2			1
Stage II	3	1		1	2	
Stage III	4	1	2	1		
Stage IV		1				
TOTALS	9	5	4	2	2	1

Among the 17 cases in Stages I and II there are 14 five-year survivals, or 82 3 per cent of those treated. There is a total salvage of 12 cases or 70 5 per cent definitely known to be alive at this writing.

The Stage III group of 30 cases shows 8 five-year survivals, or 26 6 per cent, and a total salvage of 5 cases or 16 6 per cent to date. The 28 cases in the Stage IV group produced one five-year survival, or 3 5 per cent, and 1 totally salvaged case to date,

TABLE IV RESULTS WITH DIFFERENT FILTRATION

	200 kv p 0.5 mm Cu 1.0 mm Al	200 kv p 1.0 Cu 1.0 Al	200 kv p 0.45 Sn 0.25 Cu 1.0 Al	400 kv p 0.8 Sn 0.8 Pb 1.0 Fe	85 kv p Contact Phillips*	Total
Alive 5 years						
Stage I	2		5		1	7
Stage II			3	4	1	7
Stage III			6	2	1	8
Stage IV				1		1
Per cent alive at 5 years	11%	0%	41%	35%	100%	30.8%
Dead in 5 years						
Stage I				2		2
Stage II	1					1
Stage III	7	1	7	7		22
Stage IV	8	2	13	4	2	27
Per cent dead at 5 years	89%	100%	59%	65%	0%	69.4%

* Substituted for radium therapy

or 3.5 per cent of the group. The average ages were as follows: for Stage I, 44.6 years, Stage II, 47.5 years, Stage III, 46.4 years, and Stage IV, 47 years.

The above figures do not vary too greatly from those recently reported in other clinics about the country, but we feel that it is worth while to point out one or two differences in our method of handling these cases as compared with a majority of the other institutions. The number of cases treated with the various technics are shown in Table IV, as well as the results obtained.

The majority of the cases were treated with the Thoreus filter (0.25 mm Cu, 0.45 mm Sn, and 1.0 mm Al), at 200 kv p, h v 1.19 mm Cu, 20 r per minute (in air). When using this filter, we routinely administer 1,200 to 1,600 r (in air) to each field, with a minimum of untoward skin symptoms. We feel that this is important in the treatment of these patients.

Our first aim in the treatment of any patient is the complete eradication of the disease process, but there are certain other aspects that must be considered. Ranking second to complete cure is the ability to keep the patient comfortable both during the course of therapy and afterward.

Even in the apparently hopeless case, if we can prolong life for months or years and at the same time keep the patient comfortable, we have done a good deal for her welfare as well as that of her family. At

least we are certain that we have not added to her burden such things as atrophic skin, radiation dermatitis, severe itching, sloughing, induration, and ulcerations, some of which prove to be more painful and uncomfortable than the primary disease.

Almost all of the patients seen in the Roentgenological Therapy Section have had administered 3,000 to 4,800 mg hours of radium in the usual manner, one to three weeks previously. A few of the very far advanced cases plus a few of the very early cases are given no radium therapy, depending on the findings of the referring gynecologist and the radiological consultant. The present routine technic for the treatment of a woman of average size who is referred with a diagnosis of squamous-cell carcinoma of the uterine cervix is as follows:

When the patient reaches the Roentgenological Therapy Section, seven portals are used with the indicated roentgens (measured in air) delivered to each field:

Portal	Dose r	Field Size Cm
Anterior right pelvis	1,400	20 × 20
Anterior pelvis mid line	1,400	10 × 15
Anterior left pelvis	1,400	20 × 20
Posterior right pelvis	1,400	20 × 20
Posterior pelvis mid line	1,000	10 × 15
Posterior left pelvis	1,400	20 × 20
Anterior vagina	800	8 × 10
TOTAL	8,800 r (measured in air)	

The technical factors are 200 kv p, Thoreus filter (0.25 mm Cu, 0.45 mm

Sn, 1.0 mm Al), h v l 1.9 mm Cu Only one portal is treated a day, with the daily dose of 200 r to each portal The central ray in each position is always directed toward the cervix The anterior vaginal dose is given with the patient in a modified lithotomy position and the central ray directed toward the focus of the disease with a 6×8 cm cone in contact with the vulva

The percentage depth dose with the fields and the technical factors noted above, determined both experimentally and from the literature, works out to be 55 per cent of the air dose, and the skin receives about 10 per cent fewer roentgens than where an h v l of 1.0 mm of Cu is used The tumor dose is approximately 4,800 r

To continue the ideal treatment of this case, if it is of Stage III or IV, a second series of 4,800 r in air is administered about six months later through four portals about the pelvis, with 1,200 r to each area, with the same physical factors as above In Stage I or II, if the pelvic findings show no extension following the first series, a complete abdominal hysterectomy is recommended

It should be pointed out here that for a short period near the end of this series we were in possession of a contact therapy machine and 5 patients were treated with it, 3 of whom have been followed for at least five years and are still alive The contact therapy machine was substituted for the radium, and the radiation about the external pelvis was reduced about one quarter

The ease of controlling the wave length, and thereby the penetration, as well as the direction of the central ray are decided advantages of contact therapy over radium in this disease which exists so near to such important and vulnerable structures

SUMMARY

1 There are presented the five-year end-results of an unselected series of 98 cases of squamous-cell carcinoma of the uterine cervix

2 A 76.5 per cent follow-up was ob-

tained, with an over-all five-year survival rate of 23 cases, or 30.6 per cent

3 Graphic comparison of results obtained with different filtration is presented

4 The present method of treatment is outlined, and the reasons for heavier filtration than is used in the majority of x-ray clinics are discussed

5 The advantages and results of contact therapy are mentioned

Though the series of cases is small, one is impressed with the high percentage of five-year survivals in Stages I and II In Stage III the percentage of five-year survivals is correspondingly small, and in Stage IV practically negligible

Why should there be Stages III and IV, if we can salvage more than 70 per cent of Stage I cases over five years? Is not something radically wrong from a diagnostic standpoint? There must be two very definite reasons why patients are allowed to go undiagnosed until they have extension well beyond the cervix, uterus, and into the surrounding tissues

1 Has the patient failed to consult her physician because of lack of education or lack of information regarding the seriousness of a cervical carcinoma or some of the important symptoms?

2 Does the fault lie with members of our profession? Certainly any physician has access to private and municipal laboratories which can give an accurate diagnosis from a section taken at biopsy

DISCUSSION

The work we have done has been done with the close co-operation of the Department of Gynecology and the Department of Radiology in our hospital All the patients have been seen by the gynecological service, the diagnosis has been made by the gynecologists and the pathologists

The radium treatment has been given, as is the practice in our hospital, by the gynecologists, in co-operation with the radiologists I know a great many of you

will not be in accord with this procedure. Personally, I feel that if I had one of my own who had to be treated for a cervical carcinoma, I would prefer to have a competent gynecologist apply the radium. I do not mean by that, however, that any gynecologist is competent to do radium therapy. I know we hear a great many gynecologists say "Well, put in a little radium." I think it is very important that the gynecologist who is going to do radium therapy should be familiar with radium dosage. I do not think it would be amiss for the Gynecological Board to do as we do in the American Board of Radiology—subject these gynecologists to the same form of training that we get. In other words, they should be familiar with radium and radium dosage.

Most of the cases that we are reporting

here received in the neighborhood of 3,500 to 5,000 mg hours of radium, put in by the gynecological department. The cases were treated first with radium, followed by x-ray therapy with few exceptions—some were given roentgen therapy prior to the radium.

It has been our practice in these cases to give dosage of around 8,800 r (measured in air) to six fields, giving a depth dose of about 4,500 or 4,800 r.

The voltage, as a rule, has been 200,000 volts, either pulsating or, in some instances, constant potential. A few cases were treated at 400 kv, with a composite filter, h v l 7 mm copper. With 200 kv, a composite filter has been employed, with h v l 1.9 mm copper.

St. Luke's Hospital
Chicago 5, Ill.

Dr. Ernst: Thank you, Dr. Jenkinson.

We shall now proceed to our questions and answers, first allowing the essayists to ask each other embarrassing questions. I will begin with Dr. Arneson. Do you have any questions to ask the Panel essayists?

Carcinoma of the Cervix Discussion

Dr Arneson Two questions have occurred to me. The first is in reference to Dr Siebert's paper and has to do with the histologic grading of biopsy specimens. In a single slide the pathologist may find examples of more than one particular type or grade of differentiation. The predominating form is used to classify the tumor. It should be noted, however, that the histologic appearance can be altered. One can follow the degenerative changes occurring in cervical cancer by repeated biopsy. Following irradiation there may be radical alteration without complete destruction of tumor. Recovery takes place rapidly, and evidence of renewed growth can be detected histologically. If a reasonable period intervenes between completion of x-ray treatment and the application of radium, biopsies made at that time will almost invariably reveal a more adult type of tumor than was present in the initial specimen. That change may be due to the action of radiation, or it may have been response to change in tumor environment. The question being asked Dr Siebert is whether or not there is any basis for believing that the three types he described for histologic grading may represent differences in tumor age? In other words, can a tumor begin as one type and, due to greater age or maturity, become a different type?

The second question is in reference to curability of cervical cancer. Dr Bowing reported a five-year survival rate of approximately 70 per cent among patients with early cancers. Only 6 per cent of the Group IV patients were alive at the end of the five-year period. The importance of the stage of clinical advance has been stressed as the main factor determining clinical results. If that were the only factor, we would expect all of the early cases to be cured, and we would expect no patients with advanced cancer to survive. Is the stage of clinical advance the only factor determining clinical results?

Dr Siebert As to histologic grading, I must admit that there is a great deal of difficulty. There is, however, one group which can well be separated from the others, that is the very highly malignant Grade IV tumors. About these there can be no doubt. There are also Grade I tumors concerning which there would be no marked difference of opinion. It is in distinguishing between Grades II and III that difficulty arises. Very few of these tumors would be mistaken for Grade I or Grade IV.

The importance of histologic grading of cancer is based on the fact that the more highly malignant growths metastasize earlier. Since curability in cancer of the cervix is dependent upon the extent of the tumor, or its clinical stage, and upon its histologic grade we can thus see how grading becomes of value.

Personally I am not convinced that a tumor changes its grade. I rather think that, if we see different grades in serial biopsy specimens from the same case, these various grades were present from the beginning. There is some experimental evidence that fever therapy may perhaps increase mitosis and thus make a tumor more susceptible to irradiation, but this has no practical application so far as I know.

Dr Bowing Dr Arneson's question regarding tumor advance concerns a very fundamental topic. Many interesting studies have been reported. Tumor advance is important to all therapeutic radiologists because increased knowledge of this phenomenon should result in improved methods of treatment. When the broken-dose intensive plan of radium treatment is used, one can recognize some of the gross changes in the involved field. The bleeding stops, the odor and discharge decrease, and the necrotic ulcerated surface of the lesion becomes blanched and seems to heal in much the same way as does a non-malignant ulcer. In the event of the applica-

will not be in accord with this procedure. Personally, I feel that if I had one of my own who had to be treated for a cervical carcinoma, I would prefer to have a competent gynecologist apply the radium. I do not mean by that, however, that any gynecologist is competent to do radium therapy. I know we hear a great many gynecologists say "Well, put in a little radium." I think it is very important that the gynecologist who is going to do radium therapy should be familiar with radium dosage. I do not think it would be amiss for the Gynecological Board to do as we do in the American Board of Radiology—subject these gynecologists to the same form of training that we get. In other words, they should be familiar with radium and radium dosage.

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of view of the pathologist who desires a collection of early carcinomas in order to study the problem of lymphatic extension in correlation with the histologic grade. We have little opportunity in radium-treated cases, even with serial sections, to investigate this problem. If we are to advance in our understanding of cancer, especially early cancer of a low grade of malignancy, we must have specimens that can be studied in serial section, to determine whether we are right in our opinion that such tumors are local and have not metastasized. The figures of Shields Warren on this point are striking. He found that of the low-grade squamous-cell types, only 4 per cent had metastases in the regional nodes, whereas of the transitional and fat spindle-cell types approximately 90 per cent had lymph node involvement, no matter how early the appearance on clinical or microscopic study.

I hope that I have answered Dr del Regato's question.

Dr Ernst: Dr Brewer, have you any questions?

Dr Brewer: I would like to put in a word about the statistics of Warren. They are statistics at death. Those patients were treated for carcinoma. Since they were treated, might it not be that the treatment prevented metastasis, rather than that metastasis just did not occur? To make a study of lymph node metastases in untreated carcinoma is a hard job, since most patients are treated. There are not enough untreated cases in the world to add up to statistical value.

Dr Bowing: I would like to ask Dr Jenkinson if he can state the ages of patients who had lesions that were classified as Stage I and Stage II? The results which he has reported are very good indeed.

Dr Jenkinson: No, I cannot do that.

Dr Bowing: I appreciate the possibility of error in comparing similar groups of cases, especially when the number of cases

in each group is small. In 13 of 1,491 cases of malignant lesions of the cervix in which the patients were treated at the Mayo Clinic, the lesion was classified as Stage I. The average age of the 13 patients was 59.3 years, and 70 per cent of the patients lived five or more years after the completion of treatment. In 85 of the 1,491 cases, the lesion was classified as Stage II. The average age of the 85 patients was 57.7 years, and 60 per cent of the patients lived five or more years.

There is a possibility that age alone was not the deciding factor against surgical intervention in these cases, for example, obesity and degenerative diseases may have been an added factor that would add to the risk of operation. There was no hospital mortality in these two groups of cases.

Dr Ernst: I think we had better begin answering questions from the audience. The first question is directed to Dr Brewer. Are there any 5-year survivals after surgery where lymph nodes were involved?

Dr Brewer: The answer to that is to be found in 28 patients operated upon in Stages I and II. Ten had lymph node involvement, and at the end of five years, 3 of these survived, a survival rate of 30 per cent. Among the other 18 patients, without lymph node involvement, there were 16 five-year survivals, or 88 per cent.

Chairman Ernst: Here is another question for Dr Brewer. Can surgery in Grades I and II cancer of the cervix produce as good or better five-year results than radiation therapy as outlined by Dr Bowing? If not so, then why subject the patient to surgery?

Dr Brewer: That is a good question, which, however, I cannot answer because we do not yet have an adequate group of statistics on five-year cures following surgical procedures under new conditions. They claim as good results with x-ray, they claim as good results with radium. So far, the results are only equal with surgery. In the future, however, it seems to me—and I wish to make my position clear—that in early carcinoma of the cervix—

tion of the proper radium treatment factors to meet the individual requirements of the patient, it is astonishing to observe the ultimate restoration of the previously involved structure to an apparently grossly normal state. So far, I prefer to judge the whole treatment field during the course of radium treatment rather than to observe the microscopic changes. The latter method would require the removal of multiple specimens or the removal of representative tissue from the field of treatment from time to time or at selected intervals. I am rather certain that these procedures add a definite risk and, in all likelihood, delay the treatment. We have, so far, not seen our way clear to institute the use of repeated biopsies and smears for routine study. However, we have studied the microscopic changes in irradiated tissue, chiefly in tissue irradiated before operation and in irradiated tissue removed at necropsy. In this way, the probable pattern is pieced together and it is not possible to make a complete study of each case.

MacCarty and Broders observed the presence of certain factors in their study of operative tumor tissue in the investigation of post-surgical prognosis in a variety of malignant tumors. In the main, the factors are discussed as differentiation, lymphocytic infiltration, fibrosis and hyalinization. These factors form part of a natural defense system. Various degrees of differentiation are observed only when sublethal irradiation is applied. When lethal irradiation is applied, the malignant cell is shattered, the field is chiefly made up of nuclear and cytoplasmic debris, and the resulting phagocytosis clears the way for the development of fibrous tissue and for eventual scar formation. As a rule, both lethal and sublethal effects are produced in the same field, the former in the immediate vicinity of the radium tube and the latter in distant areas. For a satisfactory local result and anatomic restoration of the involved structures with minimum scar formation, lethal irradiation effects should be kept minimal.

The grade of malignant change (Broders)

is not a guide in the estimation of the prognosis after radium therapy. This statement must be qualified, because Grade I lesions are always few in number and are adenocarcinomas, while the predominant lesion is an epithelioma.

I do not know whether I am answering Dr. Arneson's question, but to me this is probably a very, very important phase of our discussion this afternoon.

Chairman Ernst: Has any one anything to add that differs with any of these comments?

Dr. del Regato: In our experience, the League of Nations classification of carcinoma of the cervix offers the best basis for a prognosis, while the histologic grading is only of relative value. We find, however, that within the same stage those tumors with a greater degree of anaplasia have perhaps a more serious prognosis. I would like to know whether or not Dr. Siebert agrees with this view. Dr. Siebert also insisted upon his preference for surgical treatment in superficially spreading carcinomas *in situ*. I should like to know if this preference is based upon experience. Has radiotherapy failed in the treatment of these early lesions?

Dr. Siebert: First, as to prognosis in the various grades of cancer. I believe there is only one instance in which we can state that we are dealing solely with a local tumor that has not metastasized—namely, a squamous-cell carcinoma, Grade I (Broders), which has been excised with at least a centimeter of uninvolved tissue on all sides. That means, practically, that the cervix has been amputated, or at least half of it has been removed. Only on a study of such a specimen could a prognosis be made. No matter how small the tumor, if it is of Grade II, III, or IV, or of the transitional or fat spindle-cell type, I believe that it is impossible to make a prognosis as to lymph node involvement.

As to my statement that I believe that early low-grade carcinomas should be treated surgically, I speak from the point

of view of the pathologist who desires a collection of early carcinomas in order to study the problem of lymphatic extension in correlation with the histologic grade. We have little opportunity in radium-treated cases, even with serial sections, to investigate this problem. If we are to advance in our understanding of cancer, especially early cancer of a low grade of malignancy, we must have specimens that can be studied in serial section, to determine whether we are right in our opinion that such tumors are local and have not metastasized. The figures of Shields Warren on this point are striking. He found that of the low-grade squamous-cell types, only 4 per cent had metastases in the regional nodes, whereas of the transitional and fat spindle-cell types approximately 90 per cent had lymph node involvement, no matter how early the appearance on clinical or microscopic study.

I hope that I have answered Dr del Regato's question.

Dr Ernst: Dr Brewer, have you any questions?

Dr Brewer: I would like to put in a word about the statistics of Warren. They are statistics at death. Those patients were treated for carcinoma. Since they were treated, might it not be that the treatment prevented metastasis, rather than that metastasis just did not occur? To make a study of lymph node metastases in untreated carcinoma is a hard job, since most patients are treated. There are not enough untreated cases in the world to add up to statistical value.

Dr Bowing: I would like to ask Dr Jenkinson if he can state the ages of patients who had lesions that were classified as Stage I and Stage II? The results which he has reported are very good indeed.

Dr Jenkinson: No, I cannot do that.

Dr Bowing: I appreciate the possibility of error in comparing similar groups of cases, especially when the number of cases

in each group is small. In 13 of 1,491 cases of malignant lesions of the cervix in which the patients were treated at the Mayo Clinic, the lesion was classified as Stage I. The average age of the 13 patients was 59.3 years, and 70 per cent of the patients lived five or more years after the completion of treatment. In 85 of the 1,491 cases, the lesion was classified as Stage II. The average age of the 85 patients was 57.7 years, and 60 per cent of the patients lived five or more years.

There is a possibility that age alone was not the deciding factor against surgical intervention in these cases, for example, obesity and degenerative diseases may have been an added factor that would add to the risk of operation. There was no hospital mortality in these two groups of cases.

Dr Ernst: I think we had better begin answering questions from the audience. The first question is directed to Dr Brewer. Are there any 5-year survivals after surgery where lymph nodes were involved?

Dr Brewer: The answer to that is to be found in 28 patients operated upon in Stages I and II. Ten had lymph node involvement, and at the end of five years, 3 of these survived, a survival rate of 30 per cent. Among the other 18 patients, without lymph node involvement, there were 16 five-year survivals, or 88 per cent.

Chairman Ernst: Here is another question for Dr Brewer. Can surgery in Grades I and II cancer of the cervix produce as good or better five-year results than radiation therapy as outlined by Dr Bowing? If not so, then why subject the patient to surgery?

Dr Brewer: That is a good question, which, however, I cannot answer because we do not yet have an adequate group of statistics on five-year cures following surgical procedures under new conditions. They claim as good results with x-ray, they claim as good results with radium. So far, the results are only equal with surgery. In the future, however, it seems to me—and I wish to make my position clear—that in early carcinoma of the cervix—

if it is truly *early*—the treatment, primarily and fundamentally, is surgery, but that x-ray or radium should be used as adjuncts

Dr Ernst There is a question directed to *Dr Waterman* Do you treat infiltration of the rectovaginal septum with needles?

Dr Waterman Yes

Dr Ernst Have you had perforations?

Dr Waterman I do not recall any We use needles often in treating cancer of the vaginal walls, metastatic or primary

Dr Ernst Have you had any five-year cures with needles, if lymph nodes are thought to be involved?

Dr Waterman This last question is a very difficult one to answer I do not know how anybody can tell if lymph nodes are involved in the early group unless he does a Wertheim operation We have a 30 per cent survival rate in Stage III cases Almost certainly some of these patients living for five years have lymph node involvement, but we cannot tell accurately which ones

Dr Ernst What detailed information do you obtain about a Stage III and IV before starting treatment? What complications do you get? How do you handle them?

Dr Arneson An important detail of information to be sought would be the character of the growth If the cervix was surrounded with a dense collar of infiltration obliterating all fornices, and perhaps associated with extension down the anterior vaginal wall beneath an intact mucous membrane, there would be reason to believe that the tumor had been of an infiltrating quality from its beginning If there were extensive ulcerations, possibly associated with a large crater, the tumor could have begun as an everting type In all forms one would have to evaluate the degree of infection and the amount of necrosis and slough It would

also be necessary to determine whether or not an adjacent viscus were invaded

Complications in the advanced stages include persistence of tumor with extensive fibrosis and pain, post-irradiation breakdown of the tumor bed due to infection, followed by unrestrained growth of tumor, and fistula formation due to regression of cancer that had invaded the wall of a viscus

In planning treatment one would have to choose between palliation procedures and attempts to destroy completely all of the tumor In either instance it is oftentimes helpful to protract treatment over longer periods than might be employed for more favorable cases Among infiltrating types, that appears to be especially important Protraction of radium treatment is gained by using weak sources, but it is also practical to divide the treatment into multiple applications made at different intervals For any protraction of irradiation there must be an adjusted increase in the total amount of radiation

Dr Ernst Here is another question directed to *Dr Brewer* What form of treatment would you advise in a patient with cancer of the cervix who is three or four months pregnant?

Dr Brewer That is a good question I have already made a note of it to ask the others My answer is simply this When there are two such conditions present, one treats the essential disease, and the essential disease is carcinoma of the cervix Our procedure in such a patient is abdominal hysterectomy and irradiation of the cervix—irradiation with radium, followed by x-ray

Dr Ernst Someone asks *Dr del Regato* a question regarding the treatment of carcinoma of the cervical stump

Dr del Regato A very appropriate question It is well known that carcinomas developing on the remaining cervix, after subtotal hysterectomy for a benign condition, have had a relatively poor prognosis This is due to inability to irradiate them with radium as thoroughly as would

be desirable, because of the shortness of the uterine canal. In that respect transvaginal roentgen therapy constitutes a definite advantage and I believe that the prognosis of these cases will be improved with its use.

Dr Ernst Someone else—a gynecologist—asks about the position in which to examine the cervix. *Dr Brewer*, what position do you feel is best for examination of the cervix?

Dr Brewer I think that depends on what you can see, and whether you can see. We routinely examine all patients with the legs elevated and the knees bent, with insertion of a speculum. If we cannot see adequately, we do as *Dr Bowing* mentioned—turn the patient up in the knee-chest position and fill the vagina with air, which is quite easy, and may permit you to see more.

Dr Ernst Here is another question directed to *Dr Brewer*. Is there any advantage in giving the patient external radiation prior to your operation?

Dr Brewer We personally do not use it, although I can see no objection to deep x-ray therapy prior to surgery. Following irradiation we have done hysterectomies, and we find no increased technical difficulties due to such irradiation. We do believe that surgery should be preceded by irradiation of some sort, but we prefer radium.

Dr Ernst This question is directed to all of the essayists. What procedure do you recommend when there is evidence of ureteral obstruction? Would you like to answer that, *Dr Waterman*?

Dr Waterman We have adopted the practice of studying the condition of the kidney and the ureters before each case is treated. If we discover an obstruction, a hydronephrosis on one side or the other, we find out what the functional tests show. If the patient is in good shape, we are apt to start with deep x-ray therapy before we give radium. Then, at the proper time,

we go ahead and treat the lesion just as we would any lesion.

If one kidney is functioning well, we are inclined to treat the cancer and ignore the obstruction unless it is giving rise to temperature or other complications, in which case proper treatment for the condition is instituted. After all, it is a cancer that we are treating, and if the patient's condition is good, she has to take her chances on an injury. I think that, with our particular method, we miss the ureters generally.

Dr Ernst Do any of the essayists have anything to add?

Dr Bowing May I comment on the plan of routine urinary investigation? At the Mayo Clinic, we do not employ a routine urinary investigation in all cases. In cases in which the symptoms and physical findings may indicate certain urinary examinations to rule out urinary disease or complications, the selected procedures are recommended by the clinician, the therapeutic radiologist, or in consultation with the urologist. Furthermore, in all cases in which operation or irradiation therapy has been employed and further treatment is being considered, a routine urinary investigation is indicated. As a rule, the most revealing single urinary examination is excretory urography.

Serious urinary complications occur in cases in which the lesions are classified as Stage IV. In such cases, palliation is all that can be expected from a limited or cautious irradiation technic. In some cases, however, irradiation therapy will produce an astonishing improvement in the urinary complications. Our plan is to apply radium therapy to the vagina and, if possible, to the uterine cavity in limited dosage and to supplement the treatment with roentgen therapy. We have observed a small number of cases in which a good initial or early result was obtained.

Dr del Regato I would like to say in that respect that we do not think that the presence of hydronephrosis is in itself a

contraindication to treatment but that it reaffirms the necessity of starting with the external irradiation of the patient. I believe Dr S T Cantril, of Seattle, has reported two cases of marked compression of the ureter that disappeared entirely under treatment.

Dr Ernst: Here is another question. How many surgeons in the country are qualified to do operations as described by Dr Meigs?

Dr Brewer: I would not know. It amounts to this. Meigs was not qualified

when he started. Bonney was not qualified when he started. That is why I stressed, in my short presentation, that surgery should be done in good teaching research groups by a competent surgeon who will make the proper study. Cases should be sent to him so that he can rapidly accumulate numbers and also acquire technique.

Dr Ernst: I probably differ from some of the essayists who seem to feel that we have more or less reached the limit of mechanical methods for the application of radium or x-rays in carcinoma of the cervix.

Improved Methods of Intravaginal Roentgen and Radium Therapy in Carcinoma of the Cervix

EDWIN C. ERNST, M.D.

St. Louis, Mo

WE HAVE recently designed and developed several useful mechanical procedures for the irradiation of cervical cancer. At this opportune time, we wish to demonstrate the probable future significance and clinical application of these methods.

Early in 1945, after reviewing our private and clinical results at the De Paul and Barnard Free Skin and Cancer Hospitals, we realized the need for more effective and safer methods of employing larger radium dosages in the treatment of cancer of the uterine cervix. We had in mind a new type of single-unit radium applicator—one that would be more flexible and equally effective for meeting the requirements of the many different forms of distant parametrial involvement and vaginal vault extension.

Since that time we have exhibited many different models and improvements upon the originally designed combination cervical radium applicator and expanding colpostats, but the fundamental physical principle of uniform "fool-proof" spacing of the multiple radium sources or capsules has been preserved in the newer models of these applicators as shown in Figure 1.

We have clinically compared the initial erythematous and subsequent vaginal wall reactions following the use of this single unit applicator with those associated with our former "hit-and-miss" methods of indiscriminate packing of multiple radium capsules and spring colpostats, and in not a single case have we observed localized "hot spots" or tissue necrosis.

The improved uniform distribution of the radiation obtained by this method is undoubtedly due to the fact that from seven to nine radium containers are spaced

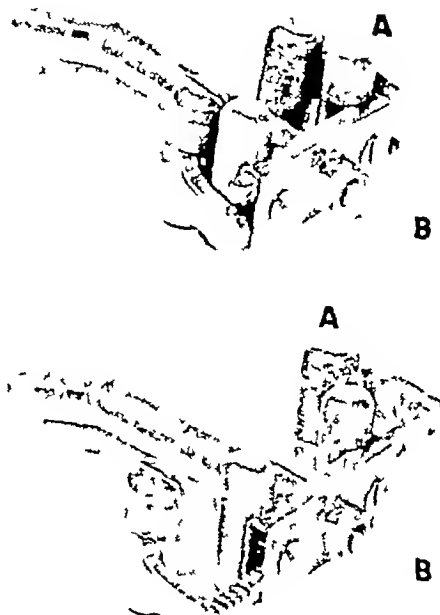


Fig 1 Expanding colpostat of the rack and pinion type in the open and closed positions. In the closed position (above) the colpostats measure 3.5 cm in width in the open position (below) 5.7 cm. The top and bottom of the vertical colpostats (A) contain the equivalent of 3 mm lead for the protection of the bladder and rectal structures. The square shaft (B) facilitates introduction and expansion of the colpostats.

In the open position the seven or more sources of radium are automatically spaced 1 cm apart

10 cm apart in both the vertical and horizontal planes. This composite radium applicator is introduced as a single unit into the cervical canal and along the cervical vaginal walls. The colpostats or radium capsules are then expanded into the fornices and parametrium, and this

¹ Presented at the Second Mexican Cancer Congress Guadalajara, February 1946 at the Second Inter-American Congress of Radiology Havana Cuba November 1946 at the Thirty second Annual Meeting of the Radiological Society of North America, Chicago Ill December 1946

fixes the positions of the seven or nine radium capsules. There is little chance for subsequent displacement or shifting of these multiple units within the vaginal vault, thus assuring greater irradiation

"rack and pinion" gear type, while Figure 2 shows another practical applicator in which there is incorporated a "lever-jack," scissor-like mechanical action for spreading the colpostats

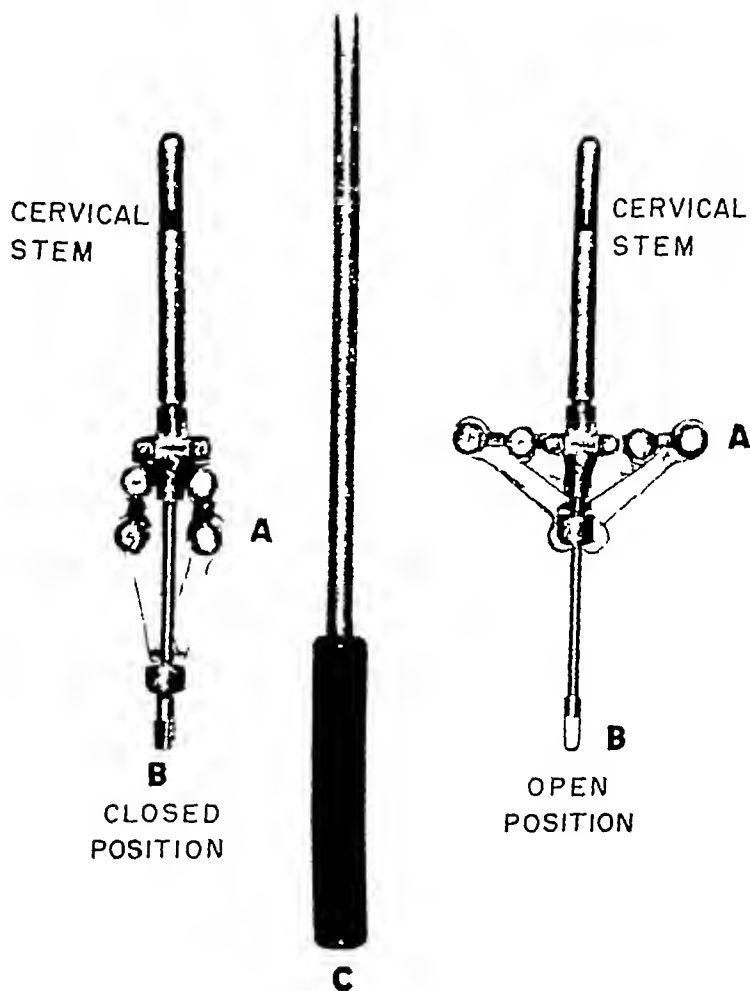


Fig 2 Expanding colpostats of the lever jack scissor like type in the open and closed positions. In the closed position the transverse diameter of the colpostats measures 2 cm. This composite colpostat may be introduced through the average speculum.

A Additional lateral colpostats may be added by means of a special attachment for increasing the expansion of the colpostats when the vaginal vault is unusually broad.

B A square shaft facilitates introduction and expansion of the colpostats. Thus all sources or capsules of radium remain 1 cm. apart.

effectiveness, with added safety to the normal structures.

Two types of expanding colpostat, illustrated here, are both mechanically controlled by long applicator rods. The radium holder shown in Figure 1 is of the

The time required for the introduction and fixation of the applicator in position is but a few seconds, rather than minutes. No special skill is necessary for the application of this holder other than the preparatory dilatation of the cervical canal.

The lateral expansion feature of the colpostats within the vaginal vault and fornices facilitates the direct irradiation of the parametrial regions. Not infrequently additional colpostats can be attached and expanded even behind the primary cervical lesion. Furthermore, the displaced cervical canal and body of the uterus in the average case can be retracted to a more central and vulnerable position, thereby enabling the expanding colpostat to assume a more effective position in closer proximity to the parametrium.

Each capsule or radiation center will accommodate three (5 or 10 mg) needles, radium cells, or a larger single radium capsule. The filtration in the cervical stem and colpostats is the equivalent of 1.0 mm platinum. The above filtration factors and diameter of the compartments within the capsules may be increased or decreased, or metallic brass may be substituted for platinum, to meet the available supply of radium or the desired specifications of the radiotherapist. The bladder and rectal fields are protected from the direct radiations by 3.0 mm of lead and 2.0 mm of brass placed within the upper and lower ends of the vaginal capsules.

For transvaginal x-ray therapy in cancer of the cervix our procedure involves the use of translucent, plastic, intravaginal x-ray cones (Fig 3) rather than opaque or metallic specula. These plastic cones can be molded to conform with the different shapes, sizes, and diameters of the vaginal vault. The lucite or plexiglass commercial tubing can thus be molded or bent into any desired shape at approximately 300 degrees while the thinner acetate butyrate tubing, when placed over the average gas stove flame or Bunsen burner, requires only 225 degrees of diffuse heat.

These plastic materials are translucent to both artificial light and roentgen rays. The lucite plastic tubing has the additional physical property of piping the artificial light along its walls, thus improving the vision of the cervical field under observation.

Even as a vaginal diagnostic procedure,

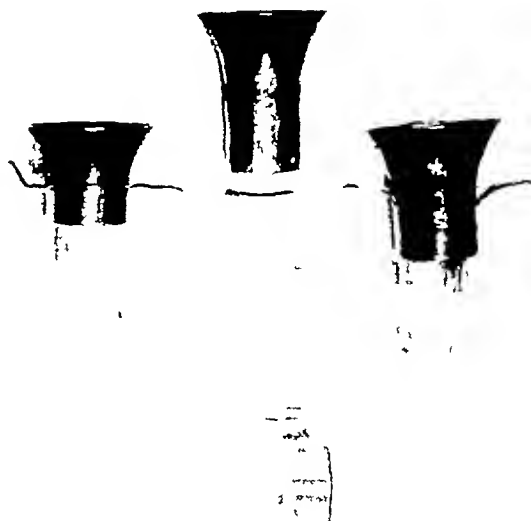


Fig 3 Transvaginal plastic translucent cones and lead-lined inserts for direct roentgen therapy. Note the different sizes, shapes, and lengths all of them tailor made to conform to the unusual vaginal vault outlines.

we prefer these plastic cones to the ordinary metallic Graves' speculum. The primary lesion and the surrounding structures within the vaginal vault can be directly outlined, and this is especially desirable for identifying certain landmarks when radiating multiple fields. Overlapping of multiple fields under these conditions can be minimized to a greater or lesser extent. Following the introduction of one of these "tailor-made" plastic cones over the field to be irradiated, this tube can be fixed to the patient by a binder or adhesive tape. Within the internal opening of the plastic cone there may be inserted short auxiliary metallic cones (Fig 3) of different lengths, depending upon the depth of the vaginal vault and the position of the urethra. The x-ray beam is then directed through this opening or lead-protected cone.

The limits of the distribution of the x-ray beam within the vaginal vault depend upon the length and diameter of the inserted lead cone, and any variations from the normal can be indirectly calculated in advance for each type of cone employed. The shorter the lead insert the broader the x-ray field

This method, in my opinion, presents added practical advantages over our past procedures of indirect (periscopic) or blind application of transvaginal x-ray therapy with metallic cone methods. A few clinical comments may be added in conclusion.

(1) In approximately 29² moderately advanced cases of cancer of the cervix a radiographic check of the position of the radium colpostat failed to disclose a single instance of displacement or shifting of the position of the radium capsules. The reverse has been our experience following insertion of many individual radium capsules in the vaginal vault.

(2) On the basis of our initial observations and clinical experience in the treatment of all stages of cancer of the cervix during the past two years, we believe that the advantages of these radium applicators

and plastic cones, as enumerated, have been fully established.

(3) If it is desirable to fractionate the radium treatment, the ease of introduction of the radium colpostat is a further advantage for daily or weekly applications.

(4) The ease and rapidity with which this radium applicator can be placed in position in the cervical canal and vaginal vault with the aid of a long-handled applicator considerably reduce the amount of radiation exposure to the operator and his co-workers.

(5) It should be emphasized that this description of the instruments and methods employed, and the mechanical and physical factors involved, is presented only as a preliminary report. Final evaluation of the clinical effectiveness of these methods is deferred for later communications.

² Twenty additional cervical cancer cases have been examined since the above presentation.

Barnard Free Skin and Cancer Hospital
St. Louis, Mo

Dr Ernst: We do not have time for any further questions, but I believe that this symposium has furnished us much material for our future guidance.

SUMARIO

Diagnóstico y Tratamiento del Carcinoma del Cuello Uterino Repaso por un Jurado

Certamen relativo a las varias fases del cáncer del cuello uterino, celebrado durante la reunión anual (1946) de la Sociedad Radiológica de Norte América

Diagnóstico Clínico
(A N Arneson)

El comportamiento clínico del carcinoma cervical varía conforme a las propiedades biológicas de la neoplasia, y en el pronóstico hay que tomarlas en cuenta, junto con la etapa de la evolución clínica y el aspecto histológico. Los tipos de proliferación externa o proyección son radiosensibles y ofrecen en general un pronóstico favorable. En estos casos el lecho del tumor puede tolerar bastante bien una irradiación de intensidad relativamente alta, pero resulta más práctico aplicar un tratamiento de menor intensidad. En las formas infiltrantes el pronóstico es malo debido a la resistencia a la irradiación y a que, al hacer el diagnóstico, frecuentemente ya están muy avanzadas. En este grupo, el tratamiento de poca intensidad resulta indispensable. Si la roentgenoterapia es prolongada o si se divide la dosis de radio en varias aplicaciones, puede alargarse la duración total del tratamiento, administrándose así dosis totales mayores. Las formas en cráter son relativamente radiosensibles, pero plantean un problema especial debido a la presencia de infección. La irradiación poco intensa esparcida durante un período prolongado resulta más eficaz en ellas que las dosis grandes administradas durante un período más breve.

Anatomía Patológica
(Walter J Siebert)

Patológicamente, puede clasificarse a los tumores del cuello uterino de acuerdo con la porción del recubrimiento escamoso de la sección vaginal del útero, en la cual tienen su origen. Por ejemplo, proceden de la capa superior los carcinomas espinocelu-

lares con su bajo coeficiente de metástasis ganglionares, de las células de transición, más profundas, los carcinomas de células de transición, y de la capa basal o germinal, los cánceres fusocelulares, con sus propiedades de invasión rápida. De estos últimos, casi 90 por ciento atacarán los ganglios linfáticos. Cada uno de dichos grupos puede subdividirse de nuevo conforme a su mayor o menor diferenciación, en Grados I, II, III y IV.

Recálcase la importancia de las biopsias en serie, sobre todo en los casos tempranos y sospechosos.

Cirugía
(John I Brewer)

El tratamiento quirúrgico del carcinoma cervical está limitado a los Períodos I y II (clasificación de la Sociedad de las Naciones) y debe emprenderse en un limitado número de casos: primero, por no obtener la radioterapia una proporción suficiente de curaciones de cinco y diez años, segundo, debido a la baja mortalidad operatoria, y por fin, por permitir eliminar posibles asientos de recurrencia. La cirugía facilita, además, tejido para examen, el cual, debidamente estudiado, debe acrecentar nuestros conocimientos del cáncer. Sólo se apoya una clase de intervención, a saber, la Wertheim, ya clásica o modificada, extirpando todo el útero, los tejidos de los ligamentos anchos y los anexos.

En la actualidad, no debe haber un cambio de frente general hacia la cirugía en el carcinoma cervical, pero sí deben emprender una justipreciación a largo plazo de este método terapéutico los cirujanos técnicamente idóneos que estudiarán su material patológicamente y observarán sus casos adecuadamente.

Curieterapia Intracavitaria
(Harry H Bowing)

La curieterapia intracavitaria, con una técnica de dosis intensas fraccionadas,

permite una amplia individualización para el mayor número de las enfermas que tienen carcinoma del cuello uterino. Esos tratamientos pueden tener por fin la curación o la paliación. La respuesta subjetiva y objetiva es bastante rápida. Con el transcurso del tiempo se han acumulado estadísticas favorables que alientan a perfeccionar esta técnica conservadora de curieterapia para el carcinoma del cuello uterino.

Se usa el tubo corriente de platino (paredes de 1 mm de grueso) que contiene 50 mg de sulfato de radio. Cada aplicador puede contener uno o más tubos. En la mayoría de las lesiones del Período III el tiempo de aplicación es de tres a veinticuatro horas, con una dosis de 300 a 2,400 mg-horas. El intervalo entre aplicaciones dura de uno a siete días. El tiempo total puede llegar a diez a veintún días. La región tratada se divide en zonas, siendo la dosis para cada zona la siguiente: zona vaginal, 2,100 mg-horas, zona cervical proximal, 1,400 mg-horas, zona cervical distal, 1,400 mg-horas, zona intrauterina, 2,000 a 2,400 mg-horas. La roentgenoterapia, iniciada algunos días antes de completar la curieterapia, se administra a través de 2 campos anteriores y 2 posteriores. 500 a 700 r a cada campo.

Curieterapia Intersticial (George W. Waterman)

El empleo de agujas largas de radioelemento con filtros de 2 a 3 mm de platino, ofrece la gran ventaja de que permite introducir el radio en los tejidos de la zona invadida. Las agujas pueden complementarse con una cápsula de platino de 20 mg de cabida, colocada en el conducto cervico-uterino. Todo el radio se deja en su sitio por espacio de 168 horas, por creerse que este tratamiento prolongado representa un factor importante en la desaparición de las células cancerosas y en la conservación y tal vez fortalecimiento de los tejidos circundantes. La técnica es sumamente flexible y fácil de aplicar, todo el tratamiento se administra en una dosis, evitán-

dose en gran parte las complicaciones debidas a la irradiación.

En los últimos 198 casos del A, la sobrevivencia absoluta de cinco años representó 38.9 por ciento. En 171 casos que recibieron la curieterapia, las curaciones de cinco años llegaron a 44.4 por ciento.

Roentgenoterapia Transvaginal (Juan A. del Regato)

Para la roentgenoterapia transvaginal del carcinoma cervical, que complementa la irradiación externa, se utiliza un espejo compuesto de una cabeza de metal destinada a proteger la vulva y de un vástago transparente a la radiación. Esto permite obtener una amplia irradiación del cuello uterino, fórnix y porciones adyacentes de los parametrios, a la vez que se resguarda, de ser necesario, la vejiga y el recto. Prefiérese una radiación de penetración moderada (140 a 150 kv), con filtros pesados (0.5 mm Cu). La distancia foco-cuello es de 25 cm. La dosis representa 3,000 a 4,000 r (en el aire) al nivel del cuello, administrada en diez a doce días.

Entre 52 enfermas consecutivas, todas las cuales, con excepción de 2, recibieron la roentgenoterapia externa, seguida de la aplicación transvaginal de rayos X, 22 estaban vivas sin signos de cáncer al cabo de tres años, o sea una sobrevivencia de 42 por ciento.

Resultados Terminales a los Cinco Años (Edward L. Jenkinson)

Preséntase el resultado terminal a los cinco años en una serie sin seleccionar de 98 casos de carcinoma céuloescamoso del cuello uterino. Pudo seguirse a 76.5 por ciento, representando la sobrevivencia global de cinco años, 30.6 por ciento (23 casos). La mayor parte de las enfermas había recibido la curieterapia—3,000 a 4,600 mg-horas—antes de la roentgenoterapia. La última se suele administrar por siete vías distintas, tratando una cada día con 200 r, y administrando una dosis total de 4,800 r. Un filtro de Thoraeus (0.25 mm Cu, 0.45

mm Sn, 1 0 mm Al) es el que ha dado meses En los Períodos I y II, sin propa-
mejor resultado En los casos de los gación después de la primera serie, re-
Períodos III y IV, puede administrarse comiéndose una histerectomía abdominal
otra serie de tratamiento al cabo de seis total

Nuevos Dispositivos para la Aplicación
de Rayos X y Radio
(Edwin C Ernst)

Descríbense, con grabados, tres nuevos
dispositivos para la irradiación del car-
cinoma cervical conos plásticos, forrados
de plomo, y diseñados de modo que se con-
formen al contorno de la bóveda vaginal,
para la roentgenoterapia directa, y dos
tipos de colpóstatos expandibles con múlti-
ples focos de radio a distancias de 1 cm



Giant-Cell Tumors of Bone¹

LT COL FRANKLIN B BOGART, M C , A U S (Inactive), and MAJ ALLISON E. IMLER M C , A U S (Inactive)

DURING THE PERIOD from Jan 1, 1942, to Oct 1, 1945, 656 patients were admitted to an army hospital designated as a radiation therapy center. Of this number, 25 had primary bone tumors, including 10 giant-cell tumors in the diagnosis or treatment of which we participated. A number of other giant-cell tumors were seen in consultation with other installations or as follow-up cases. Our opinions are influenced, also, by our experience prior to active military service and to some extent by the views of others as expressed in various publications. No statistical study will be attempted, cases presented are illustrative of certain features of the disease.

In this hospital all cases were seen by a tumor board composed of a radiologist, pathologist, surgeon, and internist, and by representatives of appropriate specialties in selected cases. The decision as to the method of treatment was made by this board.

Those desiring a review of the historical aspects of giant-cell tumors are referred to the bibliography. Important data are contained in the articles by Kolodny (20), Kirklin and Moore (19), Geschickter and Copeland (13, 14), Leucutia, Witwer, and Belanger (21), Pfahler and Parry (26), and Jaffe, Lichtenstein, and Portis (16).

METHODS OF TREATMENT

While most giant-cell tumors are benign, there is evidence to indicate that some are malignant from the outset or eventually become malignant. When tumors thought to be benign are later proved to be malignant, it would seem more reasonable to assume a lack of diagnostic acumen in the first place than to attribute malignant change to curettage, roentgen therapy, or infection. We believe that each case should be studied clinically, roentgeno-

graphically and, where possible, by biopsy. Malignant cases should be treated by radical surgical methods where the lesion is accessible. Cases that appear to be benign should be treated conservatively. Both roentgen therapy and conservative surgical methods give good results. Surgical methods, however, cannot be successfully used when the lesion is inaccessible, as in the spine or pelvis. Our personal preference is for roentgen therapy in all benign giant-cell tumors.

It has been pointed out in the past that following a series of x-ray treatments some giant-cell tumors temporarily increase in size and show an aggravation of symptoms. A period of many months is required before the final results of radiation therapy are obtained. Our experience has been that this temporary increase in the size of the tumor, with aggravation of symptoms, does occur in some cases. Instances are encountered in the literature where surgery has been resorted to within two months following roentgen therapy and the statement is made that irradiation was unsuccessful (15). Such a conclusion is not justified.

We do not believe that the roentgen doses at present advocated for children—a series of approximately 100 to 200 r delivered into the tumor and repeated at intervals of one to three months for two to four series—will cause epiphyseal damage. In some of our cases we have used much larger doses where growing epiphyses were not involved, giving as high a tumor dose as 1,500 r, with a second series of half that amount two months later. Our experience and that of many others would indicate that no better results are obtained with large doses, and we advocate using the small doses mentioned above. We agree with the previously expressed opinion (26)

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that where no damage results to skin and soft tissues, no damage will result to the epiphyses

We do not see the necessity of combining x-ray therapy with surgery in the average case. If the surgical removal of the diseased tissue is complete, postoperative irradiation is not necessary. Many have observed that cases previously treated by curettement do not subsequently respond satisfactorily to roentgen therapy, we concur in this opinion. Hence, lesions which have recurred following surgical removal are believed to be best handled by surgery if the proper surgical approach can be attained.

BIOPSY

While we feel that in many cases the roentgenographic findings will make possible a correct diagnosis, we believe that routine biopsies are desirable. With present-day surgical methods, and with bone lesions coming to biopsy relatively early in the course of the disease, there is no hazard in doing a biopsy. Correlation of biopsy data with the clinical history and roentgenographic findings should ultimately establish criteria on which to base a differentiation between benign and malignant giant-cell tumors of bone.

MICROSCOPIC PATHOLOGY

It is not within the scope of this presentation to enter into a detailed discussion of the microscopic pathology of giant-cell tumors. A careful review of the literature makes it apparent that there is no agreement among pathologists as to the etiology of these tumors or as to the relative importance of the giant cell and the stroma cell in their classification. Meyerding and Broders (24), reporting a group of seven giant-cell tumors of bone which were clinically and microscopically malignant, based their microscopic diagnosis on the appearance of the stroma cells. W. B. Coley (7) reviewed the literature and reported a group of cases diagnosed as benign giant-cell tumor from biopsy tissue and x-ray films which later underwent malignant

change. He estimated that this malignant change might be expected in as high as 15 per cent of cases.

Pathologic discussions of tissue characteristics include, in addition to the appearance of the so-called typical giant-cell tumor, a description of several variants. The variants commonly described are the spindle-cell, chondromatous, xanthomatous, myxomatous, acute giant-cell cystic (12), and an osteolytic type (12, 19). Jaffe, Lichtenstein, and Portis (16) do not believe that these variants represent giant-cell tumors and hold that when the term giant-cell tumor is restricted to the so-called typical form, malignant changes occur in a high percentage of cases. These authors also believe that, in this restricted sense, practically all giant-cell tumors will be found in patients over twenty years of age. Their classification and grading of giant-cell tumors are based upon the appearance of the stroma cells. So-called "brown tumors" are thought by them to represent only pigmented fibrous tissue scars containing osteoclasts.

The reader is referred to the bibliography for discussion of the theories of the etiology of giant-cell tumors, chief of which are the neoplastic theory, the non-neoplastic theory, and the traumatic theory.

GIANT CELL TUMORS OF THE SPINE

Four giant-cell tumors of the spine were seen. Case 1 was reported in detail in a previous communication (2). Cases 2 and 3 received their radiation therapy at this hospital. The fourth case, which is not reported in this paper, was diagnosed here and referred elsewhere for radiation therapy.

Giant-cell tumors of the spine are frequently spindle-cell variants and respond satisfactorily to x-ray therapy. It is our opinion that they are best treated by radiation alone. Recalcification of the tumor mass supports the spine, and this does not occur when the tumor tissue has been removed surgically.

CASE 1 This case was reported in detail in a previous publication (2). The patient was a male aged 20 years, who gave a history of trauma to the

neck on two occasions, eight and twelve months previous to his entering the hospital in August 1943. He had had pain in the neck for many months and just before admission numbness in the left arm had developed. X-ray examination showed destruction of the spinous process, the laminae, the inferior facet, and a portion of the superior facet of the fourth cervical vertebra. Biopsy, Aug. 27, 1943, showed benign giant cell tumor of the spindle-cell variety. One pathologist called the lesion "dysplasia of bone."

The patient was transferred to our hospital for

The factors used were the same and the estimated tumor dose was 690 r, bringing the total tumor dose to 2,070 r. This dose is larger than is usually given and, while good results were obtained, it is thought to be needlessly high.

From the time the diagnosis was first made the head was supported by a brace or a body cast. Films were made at frequent intervals. Calcification of the tumor was observed early. By March the calcification appeared complete and the brace was discarded. The pain and numbness in the left arm had disappeared by the middle of December.



Fig. 1 Case 2 Anteroposterior view showing bone production in soft tissues adjacent to pedicles of the second and third lumbar vertebrae

x-ray therapy from an overseas installation and treatment was started Nov. 3, 1943. Between that date and Nov. 13, 1,000 r were delivered to each of two lateral ports, centered over the involved area. Alternate ports were treated daily. The daily dose was 200 r and the factors used were 200 kv, added filter 0.5 mm Cu plus 1.0 mm Al, 18 ma, 28.5 r/min measured in air, skin target distance, 50 cm, h.v. 1.09 mm Cu. The estimated dose to the center of the tumor was 1,380 r.

Between Jan. 1 and Jan. 5, 1944, 500 r additional were given to each port, both being treated daily

1943, and the patient remained symptom-free after the removal of the brace. The only residual disability was slight limitation of motion of the cervical spine.

This case demonstrates that benign giant-cell tumors will respond to roentgen therapy. It also demonstrates that the calcification which takes place in a giant-cell tumor of a vertebra lends support to the spine. We believe better results are obtained when curettage is not done.

CASE 2 A white male, age 21 years, was admitted by transfer to this hospital May 18, 1945. He had received an acute injury of the lumbar spine in May 1943, having twisted his back when he stepped into a hole. X-ray films made soon after the injury were said to be negative. Since that time the patient had suffered from recurring episodes of pain which were most severe while he was lying in bed. In November 1943, he first noticed a palpable mass in the mid-lumbar region and about the same time he began to experience pain in the right hip, radiating down the right thigh. Recurrence

muscle spasm in the lumbar region. Moderate kyphos deformity and some tenderness were noted at the level of the third lumbar vertebra. There was practically no motion in the lumbar spine, limitation apparently being due to muscle spasm. Reflexes and sensation were intact.

The following examinations were normal: x-ray film of the chest, urinalysis, including Bence-Jones protein determination, sedimentation rate, red, white, and differential blood counts and hemoglobin determination, clotting time, tuberculin test, and coccidioidin skin test.

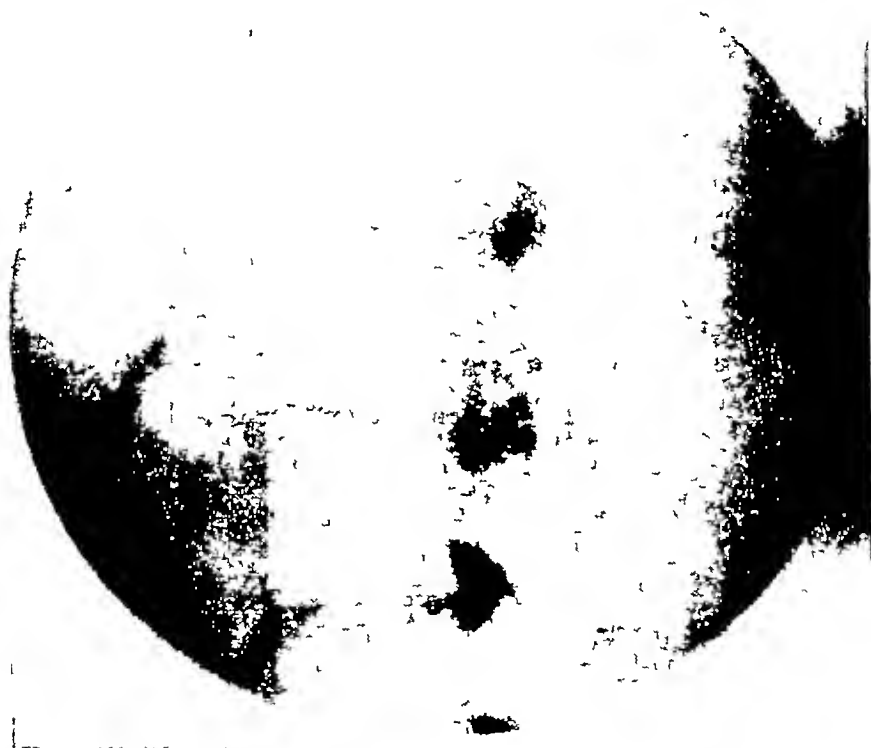


Fig 2 Case 2 Lateral view showing destruction of pedicles of second and third lumbar vertebrae. The vertebral bodies are not involved.

of the pain at various intervals finally led the patient to report on sick call in December 1944, when he received some physiotherapy. About March 1945 he again reported on sick call, at which time x-ray films revealed a lesion of the laminae of the second and third lumbar vertebrae on the right. Both transverse processes were involved, but no changes were seen in the vertebral bodies. There were both bone destruction and bone proliferation.

On physical examination the patient was found to stand with a definite lumbar scoliosis with the concavity to the right. There was marked bilateral

Our x-ray examination confirmed the observations made two months previously. The disease process involved the pedicles of the second and third lumbar vertebrae on the right side and both transverse processes. While there had been considerable bone destruction, there had also been bone production. Several large spurs of bone were visualized, extending into the surrounding soft tissue. No involvement of the vertebral bodies was demonstrated. X-ray examination of the principal bones of the body did not reveal any other lesions.

A biopsy was done May 18, 1945. The material

obtained consisted of numerous small pieces of reddish tan tissue, some containing spicules of bone. The largest piece of tissue measured $0.7 \times 0.8 \times 1.6$ cm. Microscopic sections revealed bone, connective tissue, and a small amount of muscle. Numerous bony trabeculae were seen with intervening connective tissue containing blood vessels. Areas of recent and old hemorrhage were also present. There were macrophages containing hemosiderin pigment and numerous large multinucleated giant cells averaging 8 to 10 nuclei per cell. These nuclei were round or ovoid and moderately basophilic. The cytoplasm was abundant and rather deeply eosinophilic. In some areas the bony trabeculae were surrounded by large columnar osteoblasts which rimmed the entire periphery and in some areas appeared pseudo stratified. In other areas the osteoblastic activity was much less marked, and the trabeculae were surrounded by flattened cells. There was considerable hemorrhage in the adjacent connective tissue and muscle. Scattered lymphocytes and mononuclear cells were also noted in the adjacent tissue. The histologic picture was that of giant-cell bone tumor. The giant cells, however, were smaller and had fewer nuclei than the typical giant cell tumor of bone. There was also more new bone formation than is usually seen, and the stroma was less prominent.

It was the opinion of our pathologist, Lt. Harlan I. Furringer, that the tumor was a benign giant-cell tumor. The Army Medical Museum thought that the lesion represented an ossified hematoma.

Between June 21 and July 2, 1945, 800 r of x-ray were given through a 15×15 -cm port centered over the lesion, 200 r being given every third day. The factors used were 200 kv, filter 0.5 mm Cu plus 1.0 mm Al, 18 ma, 28.5 r/min measured in air, skin target distance 50 cm, h.v. 1.09 mm Cu. The estimated dose to the center of the tumor was 776 r. The patient experienced prompt relief of pain within the first forty-eight hours and within ten days relief was almost complete. Between Sept. 5 and Sept. 17, 1945 an additional 800 r of x-ray were given, using the same factors.

The roentgenographic evidence of bone destruction and the prompt relief of pain support the diagnosis of giant-cell tumor made by our pathologist. This case illustrates the fact that good results can be obtained in giant-cell tumors of the spine when they are treated with small doses of radiation.

CASE 3 A white male, age 29, gave a history of falling during the latter part of 1942 and striking his sacrum against a crate. As a result of the accident there were some soreness and pain in the region of the sacrum for about one month. During 1943 there were complaints of vague discomfort and a sense of

fullness in the region of the sacrum. These symptoms persisted, gradually increasing, and the patient was finally hospitalized at an overseas hospital Aug. 21, 1944. Examination showed a rounded mass pressing on the rectum, apparently arising from the sacrum. X-ray study revealed destruction of the 4th and 5th sacral segments and bone proliferation which had produced a mass corresponding with the palpable tumor. A careful physical examination showed no evidence of metastases and a chest film was negative. On Aug. 24, 1944, at an overseas general hospital the tumor was surgically exposed and the coccyx and the 4th and 5th sacral segments were resected. The operator, however, felt that all the tumor tissue had not been removed. The tentative diagnosis was malignant giant-cell tumor. The description may be summarized as follows:

The specimen consisted of numerous pieces of tissue. There were several sheet like fragments of dense fibrous tissue containing bone and partly covered with tumor tissue. One mass $6 \times 2.5 \times 1.5$ cm was cystic, with walls of pale to hemorrhagic tissue. This mass of tumor tissue contained blood filled spaces. The tumor appeared to arise in the sacrum. The coccyx seemed to be intact.

Microscopic examination showed many small vascular spaces with intervening multinucleated giant cells scattered among closely packed cells with indistinct borders and elongated nuclei. Some of these stroma cells were large and hyperchromatic. There were scattered mitotic figures and scant intracellular material. In scattered foci there was newly formed atypical osteoid tissue as well as isolated spicules of fully developed bone. There were a few hemorrhagic fibrocellular areas which were free of giant cells. In these areas the cells were branching and mitotic figures were present. In many areas there were small accumulations of hemosiderin.

The patient was transferred to the continental United States and referred to our hospital for consideration of further treatment. The slide which he brought with him was reviewed by our pathologist and by the Army Medical Museum. Both made a diagnosis of *benign* giant-cell tumor, failing to confirm the earlier diagnosis of *malignant* giant cell tumor.

An x-ray film of the pelvis showed the coccyx and the 4th and 5th sacral segments missing. No evidence of tumor was seen in the stump of the sacrum. The operative scar was completely healed. Physical examination and a chest film showed no evidence of metastases. The radiologist concurred in the opinion of the tumor board that while there was no gross evidence of residual tumor x-ray therapy should be administered in view of the statement by the operator that the tumor had been incompletely removed.

Between Oct. 6 and Oct. 18, 1944, 1400 r were given through a single 15×15 -cm posterior port centered over the site of operation and including all



Fig 3 Case 4 Anteroposterior and lateral views showing trabeculated tumor in proximal end of tibia

adjacent tissue Between Nov 20 and Dec 4 1,200 r additional were delivered to the same field The daily dose was 200 r and the factors were 200 kv, added filter 0.5 mm Cu plus 1.0 mm Al, 18 ma, output 28.5 r/min measured in air 50 cm skin target distance, h v 1.09 mm Cu The total estimated tumor dose was 2,482 r We were influenced in giving such a large dose by the fact that one pathologist had thought the tumor to be a malignant giant-cell tumor A much smaller dose would probably have been as effective

The patient was followed until June 1945, x-ray films being made at intervals of a few weeks to a few months There was never any evidence of recurrence, but little or no recalcification occurred The patient remained clinically well

This case shows that good results can be obtained in benign giant-cell tumor by combining surgery and irradiation and that a moderate dose of x-rays is not contraindicated where no epiphyses are involved Recalcification does not occur when the tumor has been surgically removed Since the involved structures did not bear weight,

no harm was done in this case by surgical removal X-ray therapy was given because the operative record indicated incomplete removal of the tumor

GIANT-CELL TUMOR OF TIBIA

CASE 4 A white male, age 29, with five months of service, was admitted to the hospital May 29, 1942 His history was not remarkable except for an injury received in June 1940, when he made a sudden stop while running bases during a baseball game and severely twisted his left knee There were immediate pain and swelling of the knee and the patient was unable to walk for about four days Following the injury, he experienced slight pain and swelling of the knee and proximal third of the left leg upon excessive use There was no pain while he was at rest Radiographic examination on June 1, 1942, showed a multilocular destructive lesion, 5 X 6 X 7 cm, involving the anterior lateral aspect of the proximal end of the left tibia There was no apparent break in the cortex There was minimal lateral expansion at the superior margin of the lesion

On June 3, 1942, tissue was removed for micro-

scopic examination. The marrow was replaced by cellular tissue composed of closely packed spindle-shaped cells surrounding large giant cells. The giant cells had six to sixteen nuclei and a red, fairly abundant cytoplasm. The nuclei had a distinct, large acidophilic nucleolus and there were no mitotic figures. The spindle shaped stroma cells had a slightly smaller oval or elongated nucleus with a very small basophilic nucleolus, the cytoplasm was not distinct, the intracellular stroma was fibrillar. Scattered throughout the stroma were mononuclear, phagocytic cells containing brown pigment, undoubtedly hemosiderin. There was a moderate degree of vascularity, as indicated by numerous small endothelial lined blood vessels. These cellular structures replaced the marrow and caused considerable distortion of the bone lamellae. There were some small scattered mononuclear cells in the stroma of the tumor, probably marrow elements. In one region there was a group of large polygonal cells with characteristic vacuolated foamy cytoplasm and a small nucleus. These were modified fat or xanthoma cells. There was no evidence of malignancy. *Diagnosis* Benign giant cell tumor of bone.

Deep x-ray therapy was started June 9, 1942. Three ports, 10 X 14 cm., were used: anterolateral, anteromedial, and posterior. The ports were alternated, two ports being treated daily with the following factors: 200 kv, 0.5 mm Cu plus 1 mm Al added filtration, 20 ma, output 271 r per minute measured in air, 50 cm skin target distance, h.v.l. 0.9 mm Cu, daily dose to each treated port 200 r. Each area received a total of 1,400 r, with an estimated tumor dose of 3,200 r.

The patient was transferred to another hospital and discharged from the service April 21, 1943. A communication from him, June 22, 1945, stated that he was symptom-free. Examination of a film made in March 1945 showed considerable recalcification at the site of the tumor and no new areas of involvement.

This case was treated before either of the authors joined the radiological branch of this hospital. While the dose was larger than is usually given, no unpleasant sequelae resulted and good-end results were obtained.

CONCLUSIONS

1. Most giant-cell tumors of bone are benign, but an appreciable number become malignant or are malignant from the outset.

2. As most cases are seen before the tumor becomes massive, there are usually no contraindications to biopsy unless the lesion is surgically inaccessible.

3. Where the tumor is proved to be of the malignant type, it should be treated surgically. If the lesion is accessible it should be entirely removed.

4. For clinical purposes the variants are considered giant-cell tumors in spite of the opinion of some pathologists that they are not true giant-cell tumors. Many variants, particularly the spindle-cell variants, are located in cancellous bone, frequently in the spine. Fortunately they are usually successfully treated by radiation.

5. Tumors which appear clinically, macroscopically, and roentgenographically to be benign may be successfully treated by radiation. It is recognized that where they can be readily approached, they can also be successfully treated by surgical removal.

6. In most cases it is not necessary to combine surgery and radiation. In structures such as the spine, it seems to be a disadvantage to use curettage. Radiation alone produces calcification, which lends support to the involved area and results in an earlier cure. Cases which have been treated surgically and which recur should again be treated surgically, as they do not usually respond satisfactorily to radiation.

7. When tumors previously diagnosed as benign recur as malignant tumors, it would seem more logical to assume that the first diagnosis was incorrect than to assume that malignant changes occurred as a result of treatment, whether that treatment was surgical or radiological. There appears to be no justification for assuming that radiation as used at present induces malignant change.

8. With the comparatively small doses of x-ray used in the present-day treatment of giant-cell tumors, no damage should result to the epiphyses. A safe rule would seem to be that when there is no damage to skin and soft tissue there will be none to the epiphyses.

311 Medical Arts Bldg
Chattanooga 3 Tenn

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DISCUSSION

J Cash King, M D (Memphis, Tenn) Dr Bogart is to be congratulated upon his experience with giant-cell tumors, and particularly upon having collected these cases and obtained the follow-up while in military service. Reports of this type are of definite value in helping to establish the true role of roentgen therapy in the management of giant-cell tumors. It is hoped that more roentgenologists will report their results with this lesion. Because of my own limited experience, I am unable to add to the subject which Dr Bogart has already so ably covered, but I do want to emphasize some of the points he has mentioned.

In reference to diagnosis, it still seems important that biopsies be done prior to roentgen therapy. In this way, more complete data can be compiled, which will be of value from a statistical standpoint and helpful in establishing a more uniform method of management by roentgenologists. However, for certain inaccessible lesions, treatment must be given upon a radiographic and clinical diagnosis.

As for therapy, it seems that good conservative but thorough surgical management is the treatment of choice for accessible lesions, but for the inaccessible lesions or those in which surgical management would result in some irreparable injury to other structures, roentgen therapy is certainly indicated. As for the dosage and the interval between treatments, there is little doubt that we have a comparatively wide margin of safety, but I think all of us have used doses in excess of the minimum required to obtain the maximum benefit. The response of these radiosensitive cells to roentgen therapy is surprisingly rapid for bone lesions. Therefore, it seems advisable to keep our dosage low and study carefully the effect of various intervals between treatments. Each year seems to indicate that there is much to be learned about the interval factor in irradiation therapy of all types. Dosages of from 400 to 600 r measured in air, repeated in four to six weeks and not more than three times, have given excellent results in most cases and should not produce any injury to normal structures.

I think that it is important to emphasize that the referring physician, as well as the patient, should be thoroughly informed about the delay that is to be expected before the reparative process in the destructive lesion can be demonstrable by radiographic examination following the initial roentgen therapy. In fact, they should understand that a further progression of the osteolytic process is to be expected for a period of four to eight weeks following the initial treatment, and that this finding on radiographic examination does not mean that we are dealing with

a malignant lesion or that there is not going to be a response to radiation therapy. Furthermore, though the end-result, as shown by the radiograph, is normal, strong, serviceable bone, this is of definitely different architecture from the corresponding portion of the unaffected member. These are factors also common to the surgical treatment of the neoplasm.

The recurrences that follow surgical treatment have been reported by some authors to respond

poorly to roentgen therapy. I, personally, have had one such experience, but in that case the dosage used was in excess of that recommended at the present time. I think it advisable, however, to recommend continuation of surgical treatment once this form of management has been undertaken. The roentgenologist has the possibility of bringing discredit to roentgen therapy by applying it in such cases, and, if good results are obtained, the credit is usually given to surgery, rather than to irradiation.

SUMARIO

Osteomas de Células Gigantes

De un estudio de los tumores óseos de células gigantes observados en un Centro de Irradiación del Ejército de E U A y de las observaciones realizadas en otras partes, sácanse las siguientes conclusiones.

La mayor parte de los osteomas de células gigantes son benignos, pero una proporción apreciable o se vuelven malignos o lo son desde el principio. Cuando tumores considerados primitivamente como benignos recurren en forma maligna, es más lógico suponer que el primer diagnóstico fué inexacto que imputar la malignidad al tratamiento. Aparentemente no hay justificación para suponer que la irradiación, en la forma en que se emplea actualmente, evoque alteraciones malignas.

Dado que la mayor parte de los casos son observados antes de que el tumor se vuelva masivo, por lo general no hay contraindicaciones a la biopsia, a menos que la lesión sea quirúrgicamente inaccesible. Cuando se comprueba que el tumor es maligno, debe tratarse quirúrgicamente. Si es accesible, debe ser excidido por completo.

A pesar de la opinión en contrario de algunos patólogos, a las supuestas variantes

de estos tumores se las considera aquí puramente como tumores de células gigantes. Muchas variantes, y en particular las fusocelulares, radican en la porción reticular del hueso, y frecuentemente en el raquis, pudiendo ser por lo general tratadas con éxito por la irradiación. Varios de esos casos son comunicados en este trabajo.

Los tumores que parecen clínica, microscópica y roentgenográficamente benignos pueden ser tratados con éxito por la irradiación, y si pueden ser abordados fácilmente la intervención cruenta puede dar resultado. Por regla general, no es necesario combinar la cirugía y la radiación. En la espina dorsal el raspado parece resultar contraproducente. La irradiación, usada por sí sola, produce calcificación, la cual presta apoyo a la zona afectada y logra una curación más temprana. Las recurrencias postoperatorias no responden bien a la irradiación y deben ser tratadas con la cirugía.

Con las dosis comparativamente pequeñas de rayos X usadas en el tratamiento actualmente, las epífisis corren muy poco riesgo.

Malignant Tumors of the Small Intestine¹

HOWARD P. DOUB, M.D.

Henry Ford Hospital, Detroit, Mich

THOUGH MALIGNANT tumors occur much more uncommonly in the small intestine than in other parts of the gastrointestinal tract, they are no longer considered so rare as in the past. As a result of renewed interest in the study of the small bowel during the past decade, they are being discovered preoperatively with increasing frequency. Roentgen examination is of prime importance in their diagnosis, and generally speaking no other method approaches it in accuracy of localization and differentiation.

Tumors of the duodenum and upper jejunum are frequently discovered during routine gastric examination, but those occurring below that level usually require a special small bowel study. Roentgen examination of the small intestine is a time-consuming procedure, demanding the utmost attention to detail. The observer must constantly bear in mind the possibility of a tumor and must be alert for the roentgen signs which indicate its presence.

The procedure varies somewhat with the individual patient, but in general is as follows. On the morning of the examination, breakfast is omitted and the patient is also requested to abstain from fluids if possible. Four ounces of barium sulfate suspended in 8 ounces of water are administered, and a fluoroscopic study of the esophagus and stomach is made, as much barium as possible being forced through into the duodenum so that a complete duodenal examination can also be accomplished at this time. Fluoroscopy is then carried out at thirty-minute intervals, and films are obtained, until all the barium has left the small bowel, except when there is evidence of obstruction, in which event the time between observations and the total examination time are determined by

the motility as observed at the interval examinations. The fluoroscopic study is of the greatest value in demonstrating all of the intestinal coils and calling attention to any suspicious areas. Films are made routinely in the prone position.

Golden (4) states that he has never encountered any damage from the administration of barium sulfate by mouth in the presence of lesions of the small intestine. The small bowel contents remain fluid and can be removed by suction if necessary. A preliminary barium enema to rule out lesions of the colon is advisable in all cases with a history suggesting possible obstruction.

GENERAL CONSIDERATIONS

Pathology. Ewing (2) mentions three forms of small intestinal carcinoma: (i) a part of a local or generalized intestinal polyposis, (ii) localized adenocarcinoma with carcinomatous variations in structure, and (iii) carcinoid tumor. These tumors tend to produce various changes in the intestinal lumen depending upon their origin and mode of growth. Two principal types occur: (a) the constricting type, which consists essentially of a small, localized, infiltrating growth producing early mechanical obstruction by narrowing the intestinal lumen, (b) the fungating or polypoid type, producing a bulky mass which may project into the lumen. In the latter type there may be no destruction of the mucous membrane, obstruction is often a late occurrence and is usually due to intussusception or to the size of the tumor.

Histologically, carcinomas of the small intestine are classified under four heads: (i) adenocarcinoma, (ii) medullary carcinoma, (iii) scirrhous, (iv) colloid. Of the 34 carcinomatous tumors observed in

¹ Presented at the Second Inter American Congress of Radiology, Havana, Cuba, Nov. 17-22, 1946.

a malignant lesion or that there is not going to be a response to radiation therapy. Furthermore, though the end-result, as shown by the radiograph, is normal, strong, serviceable bone, this is of definitely different architecture from the corresponding portion of the unaffected member. These are factors also common to the surgical treatment of the neoplasm.

The recurrences that follow surgical treatment have been reported by some authors to respond

poorly to roentgen therapy. I, personally, have had one such experience, but in that case the dosage used was in excess of that recommended at the present time. I think it advisable, however, to recommend continuation of surgical treatment once this form of management has been undertaken. The roentgenologist has the possibility of bringing discredit to roentgen therapy by applying it in such cases, and, if good results are obtained, the credit is usually given to surgery, rather than to irradiation.

SUMARIO

Osteomas de Células Gigantes

De un estudio de los tumores óseos de células gigantes observados en un Centro de Irradiación del Ejército de E U A y de las observaciones realizadas en otras partes, sácense las siguientes conclusiones.

La mayor parte de los osteomas de células gigantes son benignos, pero una proporción apreciable o se vuelven malignos o lo son desde el principio. Cuando tumores considerados primitivamente como benignos recurren en forma maligna, es más lógico suponer que el primer diagnóstico fué inexacto que imputar la malignidad al tratamiento. Aparentemente no hay justificación para suponer que la irradiación, en la forma en que se emplea actualmente, evoque alteraciones malignas.

Dado que la mayor parte de los casos son observados antes de que el tumor se vuelva masivo, por lo general no hay contraindicaciones a la biopsia, a menos que la lesión sea quirúrgicamente inaccesible. Cuando se comprueba que el tumor es maligno, debe tratarse quirúrgicamente. Si es accesible, debe ser excidido por completo.

A pesar de la opinión en contrario de algunos patólogos, a las supuestas variantes

de estos tumores se las considera aquí puramente como tumores de células gigantes. Muchas variantes, y en particular las fusocelulares, radican en la porción reticular del hueso, y frecuentemente en el raquis, pudiendo ser por lo general tratadas con éxito por la irradiación. Varios de esos casos son comunicados en este trabajo.

Los tumores que parecen clínicamente benignos y roentgenográficamente benignos pueden ser tratados con éxito por la irradiación, y si pueden ser abordados fácilmente la intervención cruenta puede dar resultado. Por regla general, no es necesario combinar la cirugía y la radiación. En la espina dorsal el raspado parece resultar contraproducente. La irradiación, usada por sí sola, produce calcificación, la cual presta apoyo a la zona afectada y logra una curación más temprana. Las recurrencias postoperatorias no responden bien a la irradiación y deben ser tratadas con la cirugía.

Con las dosis comparativamente pequeñas de rayos X usadas en el tratamiento actualmente, las epífisis corren muy poco riesgo.

TABLE I TUMORS OF THE SMALL INTESTINE

	Duo- denum	Je- junum	Ileum	Total
Carcinoma	21	9	4	34
Lymphosarcoma	1	3	4	8
Carcinoid		1	3	4
Leukemia		1		1
Metastatic carcinoma	1	2	2	5
	23(44%)	16(31%)	13(25%)	52(100%)

small intestine seen in the Henry Ford Hospital (Table I), 21 were primary carcinomas of the duodenum and one a lymphosarcoma, making 42.3 per cent of the entire number. There was, in addition, one metastatic cancer. In a similar series reported by Charles Mayo (6), 26.9 per cent of the tumors were primary in the duodenum. About 90 per cent of malignant duodenal tumors prove to be adenocarcinoma. Occasionally squamous-cell or medullary carcinoma is found.

With respect to their origin, duodenal tumors have been classified by Mateer and Hartman (5) on an anatomic basis as follows: (i) supra-ampullary carcinoma, arising from the duodenal mucosa between the pylorus and the ampulla of Vater, (ii) peri-ampullary carcinoma, arising from either the papilla of Vater or the ampulla of Vater, (iii) infra-ampullary carcinoma, originating from the duodenal mucosa between the ampulla of Vater and the duodenojejunal junction. Of our series, 17 per cent were supra-ampullary, 61 per cent peri-ampullary, and 22 per cent infra-ampullary. These figures are in fairly close agreement with those of others.

The clinical picture is of considerable value in the determination of the location of the tumor in the duodenum, although a much more exact localization is obtained by roentgen study. Tumors of the supra-ampullary region often present symptoms of gastric obstruction. In the peri-ampullary group, the most common localizing sign is jaundice, which is frequently intermittent but may be continuous. Jaundice is not associated with infra-ampullary tumors, but large amounts of bile may be vomited.

Right upper quadrant pain is the most constant symptom. It may be periodic, with no relation to meals. Nausea and vomiting are frequent symptoms. Rapid and pronounced weight loss is common. In all but two of our cases the stool examination revealed evidence of occult blood. In about 50 per cent of the cases a palpable tumor is present. The liver may also be enlarged.

The roentgen findings are dependent upon the amount of deformity or constriction of the duodenum. An early tumor may escape detection if the mucosal changes are not visualized, especially in an obese patient. As the growth advances, there is usually narrowing of the duodenal lumen, with varying degrees of obstruction and dilatation of the proximal loop. This type of deformity suggests an encircling lesion. In some cases there is a characteristic filling defect produced by a more localized bulky tumor or by an ulcerative lesion in one wall of the bowel. Reverse peristalsis is common if any degree of obstruction is present. Gastric retention of varying degrees is of frequent occurrence and in some instances may lead to a mistaken diagnosis of simple pyloric obstruction. The duodenum may show an exaggerated curve downward and to the right. Displacement of the stomach upward and laterally may be a secondary pressure effect. Tumors in the distal duodenum are often large and the defects resemble those in the upper jejunum.

Sometimes no localizing defects are demonstrable roentgenologically. In some of these cases the tumor involves the papilla of Vater but has not progressed to the extent that duodenal deformity results. Of our series of 21 cases, 12 showed definite localizing defects. In 4 patients an obstructive lesion was found, with high-grade gastric retention and various atypical deformities which were not definitive as to location. The findings in 3 cases were entirely negative, and 2 patients were not examined roentgenologically. In one of these last the tumor was discovered post-mortem and in the other at operation.

the series upon which the present paper is based, more than 90 per cent were adenocarcinomas. The medullary type is next in incidence, while the other types are rare.

The lymphoblastomas may occur anywhere in the small intestine but show a predilection for the ileum. They usually produce a diffuse infiltration, involving one or more segments of the bowel. They are generally intramural growths and may not destroy the mucous membrane until late. Obstruction is not a striking feature and between areas of constriction there may be areas of actual dilatation.

Except for the lymphoblastomas, sarcomas of the small intestine are uncommon. When sarcoma does occur, it is usually a pure or mixed fibrous or spindle-cell type.

Argentaffine or carcinoid tumors resemble carcinoma histologically and are differentiated only by the silver impregnation method of staining, which demonstrates the presence of argentophil granules. In many instances these tumors are benign and are discovered only at autopsy, but occasional examples exhibit the characteristics of malignant neoplasms.

Clinical Picture The rapidity of development of the clinical signs and symptoms depends largely on the location of the tumor and the degree of obstruction which it produces. There may be a history of progressive weakness and loss of weight with bowel irregularity, sometimes extending over a period of months. Varying degrees of anemia may occur, and stool examination will usually show evidence of blood.

In many cases pain is an outstanding symptom. It may be intermittent, and of a sharp, colicky nature. Its location varies with the location of the tumor. Nausea and vomiting are frequently present. Constipation is common and is the rule in those cases showing obstruction. Examination will often reveal a palpable tumor, and there may be distention, depending upon the amount of obstruction present. Evidence of peristaltic activity with gurgling and rumbling may be observed.

In general two clinical pictures are seen. In the first, the signs and symptoms are regional, dependent upon the location of the tumor and the degree of mechanical alteration in bowel function. In the second, the changes are constitutional in their effect. These clinical manifestations will be dealt with more specifically in discussing tumors of various parts of the intestine.

Roentgen Findings The roentgen signs of tumor of the small intestine are largely those observed in tumors of other parts of the gastro-intestinal tract. Where obstruction has not taken place but there is encroachment on the lumen, either extrinsic or intrinsic, various types of deformity or filling defects, such as are seen elsewhere, will be demonstrable. The growth may be annular, producing the familiar narrowing or constriction of the bowel, usually with an accompanying dilatation of the proximal loops. In some cases there is a marginal defect or even one of central type, depending upon the point of origin and development of the tumor. In most instances where the growth has become large enough to be detected roentgenologically there will be obliteration of the mucosal pattern, even though the point of origin is in the submucosa and there is not actual invasion of the mucous membrane. Fluoroscopic examination is of great importance in visualizing the mucosal pattern of the affected area and in many instances will give the clue that differentiates tumor deformity from non-tumor deformity. In certain cases the examiner is unable to determine the exact nature of the process and must be content with the diagnosis of an obstructing lesion.

TUMORS OF THE DUODENUM

Primary malignant tumors of the duodenum are relatively uncommon, but can not be called rare. They constitute about 3 per cent of all cancers of the gastro-intestinal tract. We have found the duodenum to be involved by malignant new growth more frequently than any other segment of the small bowel. Of a series of 52 proved malignant neoplasms of the

either the cause or location of the obstruction. During the routine small bowel study the most valuable sign is stasis of the barium due to partial or complete obstruction. This may occur in a single area or in multiple areas, as in lymphoblastoma. When the obstruction is complete, the distal end of the barium column often has a rounded or bulbous contour and the bowel proximal to it is dilated. In cases with partial obstruction small amounts of barium can be seen to trickle past the narrowed area. In some cases a typical filling defect will be demonstrable, the result of a tumor projecting into the lumen of the bowel and encroaching on the normal opening. Tumors of the mesentery and intramural tumors may produce deformity of the normal outline, with obliteration of the mucosal pattern, even though they do not actually invade and destroy the mucosa. This is due to pressure of the bulky mass.

Swenson (8) advocates decompression with the Miller-Abbott tube followed by injection of small amounts of barium. With this procedure small lesions are not obscured by overlying loops of barium-filled bowel and their location and probable nature can be more accurately determined. While this technic is undoubtedly valuable in certain cases, in many instances the routine small bowel examination will suffice.

CASE II. F W, a white male, aged 38, complained of nausea and vomiting which had become more severe during the ten days prior to admission. He had lost 33 pounds during the past month. In the same period there had been jaundice for ten days, increasing weakness and loss of appetite. Constipation had been severe for one week.

Physical Examination. No palpable masses were present. There was no spasm or tenderness. The liver was not enlarged. Blood studies were normal. Stool examination (guaiac test) was positive for occult blood (4 plus).

Roentgen Examination. Roentgenograms of the stomach were normal. There was almost complete obstruction of the upper jejunum by a tumor. Narrowing of the lumen suggested an annular growth. There was considerable retention at the time of the six hour examination (Fig 2).

Operation. An annular growth was found in the jejunum about 3 feet distal to the duodenum. The



Fig 2 Case II Annular carcinoma of the jejunum causing almost complete obstruction

proximal bowel was markedly dilated and the distal bowel collapsed. There were enlarged mesenteric lymph nodes in the vicinity of the tumor. The jejunum containing the tumor was resected together with the enlarged nodes. The pathological diagnosis was adenocarcinoma, grade II. The regional nodes showed evidence of neoplastic tissue.

CASE III. G A, a white male, aged 58, complained of general weakness for two months with a loss of weight of about 45 pounds. He had had some fever during the past two weeks, the temperature reaching 101° F. Diarrhea had been present for one week, but no blood had been observed in the stool.

Physical Examination. There was some rigidity in both upper quadrants of the abdomen. No palpable masses were present. The chest findings were normal.

Laboratory Examination. Blood studies showed hemoglobin 11.2 gm, red blood cells 3,600,000, white blood cells 4,900 (61 per cent polymorphonuclears, 39 per cent small lymphocytes). The urine was negative. The stool was positive for occult blood (guaiac test 4 plus), stool culture was negative for tubercle bacilli.

Roentgen Examination. The stomach was smooth in contour. The duodenal cap filled well. The duodenum and upper part of the jejunum were dilated, with a large irregular filling defect in the

CASE I L H, a white female, aged 55, had gastro intestinal symptoms beginning two years prior to admission, with vomiting and abdominal distress. One year later vomiting again occurred. Black stools were frequent. There had been a weight loss of 30 pounds during the last eight months.

Physical Examination Emaciation was prominent. The skin was yellowish. There was considerable tenderness over the upper epigastrium. The liver and spleen were not palpable.

Laboratory Examination The hemoglobin was 61 per cent, red blood cell count 4,300,000, white blood count 6,450. Urinalysis was negative. The Wassermann reaction was negative.

Roentgen Examination The stomach and duodenal cap were normal. In the second portion of the duodenum was an area of constriction suggesting an organic lesion, possibly malignant in origin. There was marked 6 hour gastric retention. A later examination showed an irregular filling defect suggesting a malignant lesion (Fig. 1).

Operation Posterior gastroenterostomy was done. The patient was found to have a peri ampullary primary carcinoma of the duodenum, with metastases in the liver and head of the pancreas.

TUMORS OF THE JEJUNUM AND ILEUM

Tumors of the jejunum and ileum produce a similar clinical and roentgenologic picture and will be considered together. Jejunal tumors constituted 27 per cent of our series and included 9 carcinomas, 3 lymphoblastomas, 1 case of leukemic infiltration, and 1 carcinoid tumor. In the ileum there were 4 carcinomas, 4 lymphoblastomas, and 3 carcinoids, constituting 21 per cent of the total series. Four metastatic tumors (2 of the jejunum and 2 of the ileum) were also found.

In the presence of tumors of the jejunum and ileum the clinical symptoms are those of obstruction, due either to intussusception or blocking of the intestinal lumen by the mass of new growth. Obstruction attributable to intussusception is of sudden onset with acute pain and vomiting, blood may be passed by rectum, a sausage-shaped mass is usually palpable, and the abdomen is distended. Obstruction due to encroachment of the growing tumor on the lumen produces different clinical manifestations. The onset is gradual. For several months the patient has a vague feeling of abdominal uneasiness, with belching, bloating, and some



Fig. 1 Case I Peri ampullary primary carcinoma of the duodenum

pain. As the tumor becomes more obstructive, pain assumes a more prominent place in the picture. It is frequently sharp, colicky, and intermittent. The site is the median line above and below the umbilicus. Nausea and vomiting are often late symptoms but are rather constant when obstruction is present.

Physical examination usually shows evidence of weight loss, sometimes to the point of emaciation. The most significant finding—if distention is not too great—is a palpable tumor. In other cases, when no tumor can be palpated, a sense of resistance is encountered. Tenderness is not a prominent sign.

Secondary anemia is the rule in malignant tumors of the jejunum and ileum. Stool examination is usually positive for occult blood.

A film of the abdomen may show evidence of small bowel dilatation, but this does not give exact information regarding



Fig 5 Case IV Adenocarcinoma of the terminal ileum and cecum

rant, the abdominal organs were not palpable. There was some distention.

Laboratory Examination The stool examination showed occult blood (guaiac test 4 plus). The blood examination was negative.

Roentgen Examination The stomach was negative. There was evidence of partial small bowel obstruction, probably in the ileum. This persisted over a 48 hour period, and the possibility of a tumor was considered (Fig 6).

Operation Operation revealed dilated loops of small intestine with an area of narrowing in the lower ileum, due to tumor growth. The mesenteric nodes were enlarged. Complete resection of the involved area was carried out (Fig 7).

Pathological Report Adenocarcinoma, grade 3.

LYMPHOBLASTOMA

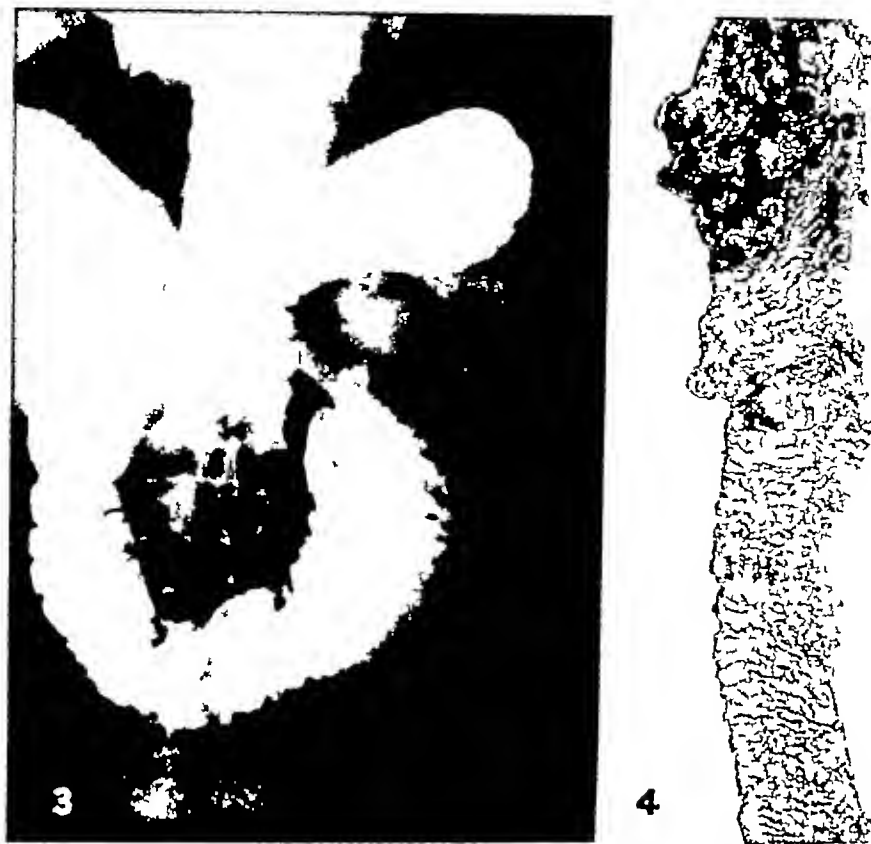
Lymphoblastomas are not rare, comprising about 1 per cent of all malignant gastro-intestinal tumors. There were 8, or 15.4 per cent, in our series of 52 cases. They are most common in the ileum but may occur in any of the segments of the small bowel and are frequently multiple. Males are more frequently affected. The highest incidence is in the fourth decade.

The most common complaint is vague



Figs 6 and 7 Case V Adenocarcinoma of the lower ileum causing dilatation and narrowing

diffuse abdominal pain, usually unrelated to food intake or bowel function. Since these tumors originate in the submucosa, they may attain large size before destroying the mucous membrane or invading the peritoneum. For this reason, hemorrhage from the bowel and peritoneal irritation may be late symptoms. There is often a change in bowel habit, with alternating diarrhea and constipation.



Figs 3 and 4 Case III Leukemic lesions of the upper jejunum

jejunum just distal to the dilatation. This suggested a tumor of the bowel causing partial obstruction (Fig 3). There was six hour retention in the stomach and bowel proximal to the tumor.

Operation and Subsequent Course At laparotomy a large tumor was found in the upper jejunum and several smaller masses were palpable (Fig 4). The section of the bowel containing the tumors was removed. Later the patient passed blood by rectum. He also vomited blood and a generalized purpura developed. Blood studies on the last day of life showed hemoglobin 9.5 gm, red blood cells 3,230,000, white blood cells 12,800 (57 per cent polymorphonuclears, 40 per cent small lymphocytes, 3 per cent monocytes).

Necropsy At necropsy there was evidence of myelogenous leukemia (aleukemic stage) with leukemic infiltration of the heart, liver, spleen, small intestine, adrenals and kidneys. There was generalized purpura with hemorrhages in the intestine.

CASE IV A. D. a colored female aged 46 complained, on admission, of cramping abdominal pain, nausea, and vomiting. The pain was more pronounced about two hours after meals and the attacks had recently become much more frequent and severe. There had been a weight loss of 15 pounds during recent months.

Physical Examination Palpation disclosed a firm rounded mass, about 4 × 6 cm, in the right lower abdomen in the para umbilical area. There was no abdominal distention or tenderness. Blood studies were essentially normal. A guaiac test of the stool was negative.

Roentgen Examination Small bowel studies revealed evidence of narrowing of the terminal ileum just proximal to the ileocecal valve. There was partial obstruction of the bowel, with barium remaining in the ileum proximal to the point of obstruction for more than twenty-two hours. This suggested the presence of a malignant tumor of the terminal ileum and cecum (Fig 5).

Operation A tumor of the terminal ileum and cecum was found. Large metastatic nodules were present in the liver. The pathological diagnosis was adenocarcinoma, grade 3.

CASE V M. T. white female aged 40 complained of general weakness and increasing constipation relieved only by saline enemas. Generalized abdominal cramps with nausea and vomiting had appeared recently. There had been a weight loss of 20 pounds over the past year.

Physical Examination Chest examination was negative. In the abdomen a small, hard subcutaneous nodule was palpable in the right upper quad-

they are discovered only at operation, as non-obstructing nodules. The literature, however, contains numerous reports of carcinoids resembling other malignant tumors and metastasizing widely. Two of our patients showed definite defects roentgenologically and partial obstruction. In one case roentgen findings were negative and in one case the small bowel was not examined.

SUMMARY

The recognition of malignant tumors of the small intestine depends upon a careful evaluation of the clinical features, including laboratory studies, and, most important of all, a careful roentgen study. Much of the improvement in the recognition of these tumors has resulted from the more widespread use of serial study of the small bowel during the past decade. Newer refinements in technic can be expected still further to increase the accuracy of diagnosis.

The highest percentage of malignant neoplasms of the small bowel are adenocarcinomas. Lymphosarcomas are second in numerical order and carcinoid tumors a poor third. Grossly the tumors are of two types: constricting and fungating or polypoid. The constricting type produces mechanical obstruction by narrowing the intestinal lumen, while with the polypoid type obstruction is due to the bulk of the tumor or to intussusception.

The clinical picture is usually one of a progressive loss of weight and strength and varying degrees of anemia. Pain is a prominent symptom. A change of bowel habit is usually present and this may go on to an acute obstruction which brings the patient to seek relief. A palpable tumor is an important and significant finding. Distention is often present. Unusual peristaltic activity is common.

The roentgen picture is one which is common to the neoplasms of the gastrointestinal tract. The abnormal findings may consist of an area of narrowing of the lumen of the bowel and dilatation proximal to it. Marginal or central filling

defects may also be present, with obliteration of the mucosal markings in the involved area.

Our series of 52 malignant tumors of the small intestine includes 21 carcinomas of the duodenum and 1 lymphosarcoma, or 42.3 per cent, 17 per cent of these tumors were in the supra-ampullary portion of the duodenum, 61 per cent were in the peri-ampullary portion, and 22 per cent in the infra-ampullary portion. Varying degrees of obstruction of the duodenum and stomach are commonly found associated with duodenal tumors. In the peri-ampullary type, jaundice, often of an intermittent character, is a prominent feature and is dependent on the degree of obstruction of the ampulla. Pain is the outstanding symptom. In about 50 per cent of the cases a palpable tumor is present. The roentgen signs vary from irregular constriction of the lumen with obstruction to filling defects due to a bulky tumor or an ulcerative lesion. Secondary duodenal displacement, peristaltic reversal, and gastric retention are found. Metastasis to the regional lymph nodes and nearby organs is common.

The symptoms and roentgen signs of jejunal and ileal tumors are similar. Our series included 14 primary malignant tumors in the jejunum, or 27 per cent of the total. In the ileum there were 11 primary tumors or 21 per cent of the total. In these areas the clinical syndrome is usually that of obstruction, produced either by intussusception or by tumor growth. The symptoms may be acute and constitutional in the case of intussusception or gradual in the case of a slow growing tumor. Loss of weight and strength combined with anemia and a palpable abdominal tumor are suggestive signs. The roentgen examination will usually disclose evidence of partial or complete obstruction with dilatation of the proximal bowel. A typical filling defect may be present. Mucosal alteration is present as a result of invasion or pressure defect.

In addition to the primary carcinomas, there were 5 metastatic cancers (1 in the



Figs 8 and 9 Case VI Lymphosarcoma of the jejunum and ileum

Acute obstruction is not common, since the growths are rarely of the annular type. Occasionally intussusception may cause obstruction. Stasis may be due to involvement of the submucosal nerve plexus, with consequent disturbance of the autonomic nerve control of the bowel.

The types of deformity and filling defects seen on the roentgenogram are those described above. In addition, one occasionally sees a large localized dilatation of the bowel with narrowing in other areas, accompanied by partial obstruction. This is the result of ulceration combined with obstructive effects to produce an aneurysmal-like sac. This picture is characteristic of lymphosarcoma but is not common.

CASE VI. M. F., a white female, aged 62, complained of attacks of diarrhea and fever for the past seven years, with moderate abdominal pain and some bloating. The weight loss over this period was 30 pounds.

Physical Examination. A hard, somewhat tender mass was palpable in the left umbilical area. There

was no general adenopathy. Stool examination was positive for occult blood (guaiac test 4 plus). Blood studies showed a mild anemia.

Roentgen Examination. The small bowel study showed an unusual mucosal picture. There were areas of deformity, with widening of the lumen in some places and narrowing in others. Some areas suggested the presence of intramural tumor and others pressure defects. The findings were suggestive of lymphoblastoma (Fig. 8).

Operation. Two areas of new growth were found, one in the jejunum and one in the ileum, in the right lower quadrant. A few enlarged mesenteric nodes were present. The involved areas were resected. The pathological diagnosis was lymphosarcoma (Fig. 9).

CARCINOID TUMORS

Attention has already been called to carcinoid tumors in the discussion on general pathology. These tumors are rather uncommon. They occurred only 4 times in our series of 52 cases (7.5 per cent). They are most frequently found in the ileum but may occur in other parts of the small intestine. In some instances

En esta serie hubo 8 linfosarcomas, siendo más frecuentes en el ileon, aunque pueden presentarse en cualquiera de los segmentos del intestino. La obstrucción aguda no es habitual, dado que el desarrollo es frecuentemente intramural más bien que intraluminal. Roentgenológicamente, los linfosarcomas caracterízanse a menudo por

zonas de estenosis, adyacentes a otras de dilatación. De cuando en cuando nótase una típica dilatación localizada en forma de aneurisma.

Observáronse 4 tumores carcinoideos, en 2 de los cuales había nichos y obstrucción parcial. En un caso el examen radiológico resultó negativo y en otro no se ejecutó



duodenum and 2 each in the jejunum and ileum), 10 per cent of the entire series

Lymphosarcoma occurred 8 times in this series, representing 15.4 per cent of the total. It is most common in the ileum but may occur in any of the segments of the intestine. Acute obstruction is not common, as the growth is frequently intramural rather than intraluminal. Roentgenologically lymphosarcomas are often characterized by areas of narrowing and adjacent areas of dilatation. A characteristic aneurysmal-like localized dilatation is occasionally present.

Carcinoid or argentaffine tumors occur most commonly in the ileum and appendix but may be found in other parts of the gastro-intestinal tract. These are frequently of low-grade malignancy but may show evidence of metastasis and other signs of malignant growth. There were 4 cases in our series, 7.5 per cent of the total. In 2 of these cases there were filling

defects and partial obstruction. In one case roentgen examination was negative, and in one no roentgen study was made.

The Henry Ford Hospital
Detroit 2 Mich

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SUMARIO

Tumores Malignos del Intestino Delgado

En la serie de 52 tumores malignos del intestino delgado, estudiada, había 21 carcinomas y 1 linfosarcoma del duodeno. De las neoplasias duodenales, 17 por ciento se hallaban en la porción supra-ampular, 61 por ciento en la peri-ampular y 22 por ciento en la infra-ampular. Por lo general se asociaba con los tumores duodenales obstrucción en mayor o menor grado del duodeno y estómago. En la forma peri-ampular, la ictericia, a menudo intermitente, constituye una característica notable, dependiendo de la mayor o menor obstrucción de la ampolla de Vater. El dolor es el síntoma sobresaliente. Aproximadamente en 50 por ciento de los casos el tumor es palpable. Los signos roentgenológicos varían de construcción irregular de la luz intestinal con obstrucción a nichos debidos al volumen del tumor o a una lesión ulcerada. También se observan desplazamiento secundario del duodeno, inversión del peristaltismo y retención gástrica. Las metástasis en los ganglios

linfáticos regionales y los órganos adyacentes son frecuentes.

La serie comprendía 14 cánceres primarios del yeyuno y 11 del ileon. En dichas zonas el síndrome clínico suele ser el de la obstrucción, producido bien por la invaginación o la proliferación del tumor. Los síntomas pueden ser agudos y orgánicos, tratándose de invaginación, o paulatinos si se trata de una neoplasia de desarrollo lento. La pérdida de peso y de fuerzas, combinada con anemia y un tumor abdominal palpable, son signos indicativos. El examen roentgenológico suele revelar signos de obstrucción parcial o completa con dilatación de la porción proximal del intestino. Puede existir un nicho típico. La alteración de la mucosa proviene del efecto de la invasión o presión.

Además de los carcinomas primarios, observáronse 5 metástasis cancerosas (1 en el duodeno y 2, cada uno, en el yeyuno y el ileon), representando 10 por ciento de toda la serie.

Further Observations with Intravaginal Roentgen Therapy of Cancer of the Female Pelvis¹

W WALTER WASSON, M.D., and ROY GREENING, M.D.

Denver, Col

THE PURPOSE OF this paper is not to relate the successes of a new method for the roentgen treatment of carcinoma of the pelvis, but rather to discuss some of the failures of this form of therapy and to offer certain procedures with the hope of better end-results. It can be said that almost any method of treatment—radium, roentgen therapy, or surgery—will cure cancer of the cervix in the First Stage. It is in the Second, Third, and Fourth Stages of this disease that any of these methods, or all of them combined, have their percentages of failures.

The ultimate goal of the radiologist is twofold that is, to produce a dosage of radiation uniform in distribution throughout the pelvis and of an intensity adequate for destruction of the cancer cells. It is an essential premise that the cancer cells must have a lesser resistance than the tumor bed or the surrounding tissue. The mechanical facilities for the production of such uniform dosage of radiation are available.

ANATOMY

Of primary importance is an intimate knowledge of the anatomy of the female pelvis, of the sites for the beginning of cancer, and of its methods of dissemination. The anatomical structures so involved lie almost entirely within the birth canal (Fig 1). While the canal possesses known variations in size and shape, it is in general a short cylinder, in the center of which are the bladder, uterus, and rectum and some intestinal viscera and their lymphatics, while near the outer walls are the ovaries and numerous lymph nodes (Fig 2). Surrounding this birth canal are the bony pelvis and its muscles and ligaments, and external to the bony pelvis are the struc-

tures of the thighs, buttocks, and abdomen. It is these latter anatomical structures that distort the measurements of the female pelvis and provide a confusing obstacle to its uniform irradiation. Even in an apparently Second-Stage cancer of the cervix of a Grade III type, the cancer cells may already have passed into the lymph nodes along the lateral walls of the pelvis, and thereby account for some of the failures where the roentgen and radium therapy is inadequate in its distribution.

DIAGNOSIS

The approach to the diagnosis of cancer of the cervix and pelvis should be made with the same care and planning as that for any major surgical operation. Too often, under the pressure of a busy office or clinic, insufficient time is given to the consideration of the stage and grade of involvement and the technical procedures necessary for the destruction of the cancer. Each stage of involvement requires a different technic for the best result. No one routine technic of irradiation can be correct for all types and stages of involvement. Insufficient emphasis has been put upon this fact by many radiologists, including the authors. Cancer of the cervix so often presents itself so frankly, and the diagnosis is made so easily, that the radiologist may proceed with his treatment without due consideration of the possibility of more extensive involvement than is apparent upon the first examination.

In making the diagnosis, a careful examination of the pelvis is the first essential. As mentioned by many authors, this examination should be done with the greatest caution. Undue pressure in the manipulation of the pelvic organs is contraindicated.

¹ Presented at the Thirty second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

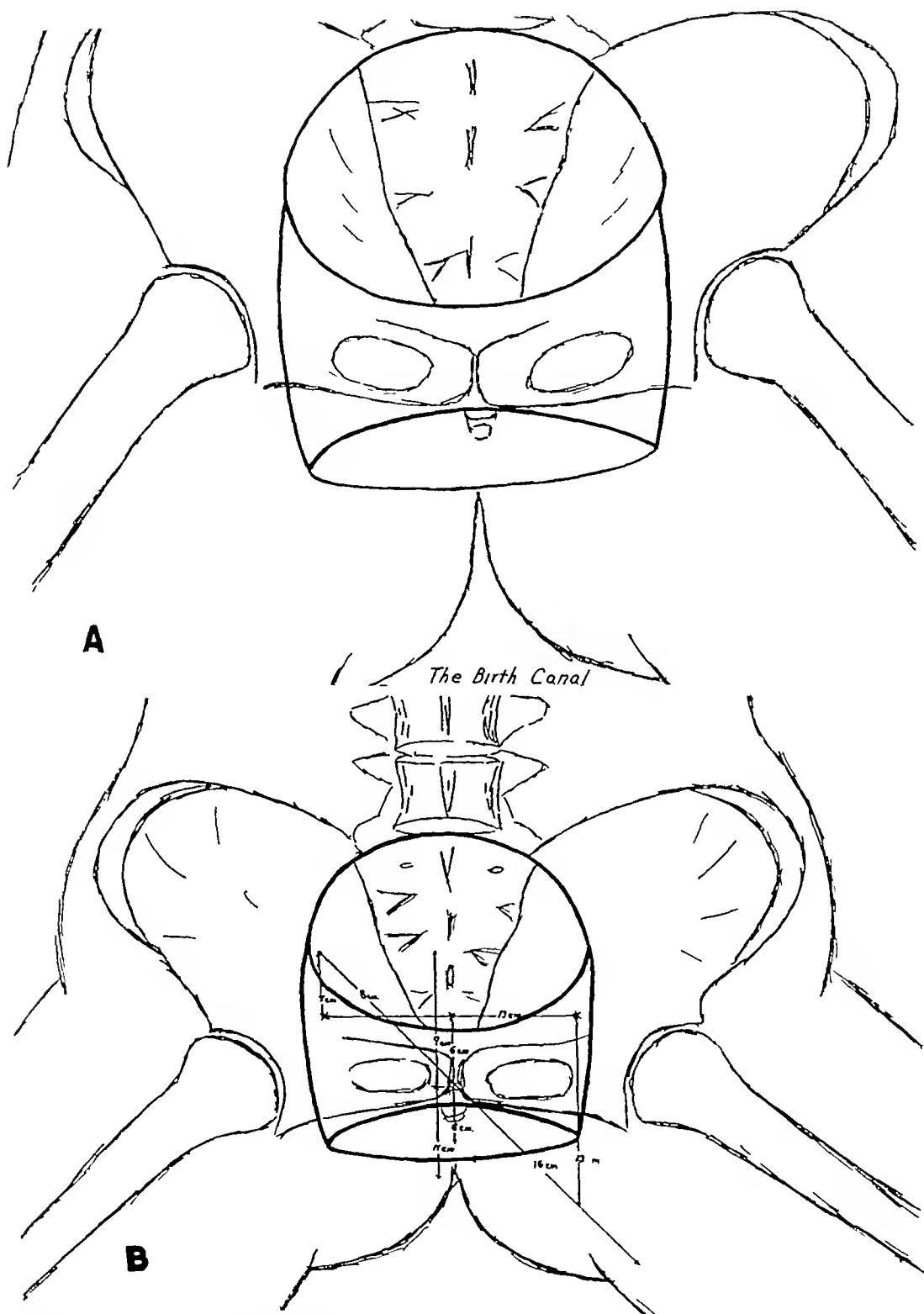


Fig 4 A Diagram showing relationship between the birth canal which contains the female organs, and the surrounding structures
 B Illustration showing the necessity of measuring each female pelvis for computing the tumor dose delivered through any one port

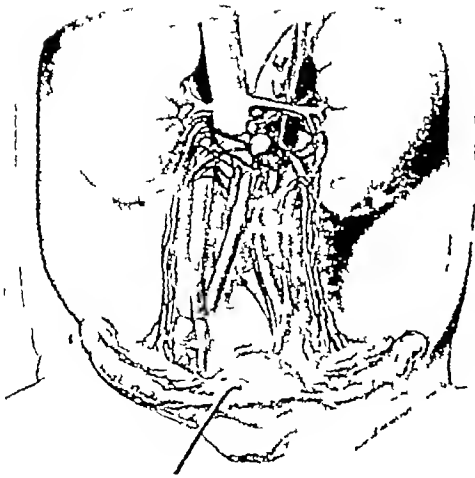


Fig 2 Uterus, ovaries, and a few of the numerous lymphatic channels and nodes (Reproduced from Bartels)

and dangerous because of the possibility of thereby expressing the cancer cells into the lymphatic channels. For this same reason, curettements and lipiodol injections of the uterine cavity, while very essential to an accurate diagnosis of the cervical canal and uterus, must be done with the greatest care and be reserved for those cases only in which such a procedure is necessary. On the other hand, a biopsy is not only very desirable but can be done without risk to the patient. The discharge coming from the uterus and cervical canal is of the greatest diagnostic significance.² A purulent discharge should warn the radiologist of the probability of uterine involvement even when the cancer appears to be limited to the cervix. Constriction of the cervix with retention of the uterine secretions and subsequent enlargement of the uterus may also confuse the diagnosis. A roentgenogram of the pelvis is not of value in making a diagnosis of cancer of the female pelvis, but is useful for localization of the female organs in an obese patient. This is especially true where intravaginal roentgen therapy is to be given and uniform radiation from small cones is obligatory.

* The vaginal smear as developed and perfected by Papanicolaou and advocated by Meigs and R. Graham is of great value and often it is diagnostic.

TREATMENT

Having made the diagnosis as to the type of cancer, the grade and the stage of involvement,³ the radiologist is then ready to select his method of treatment. The question of treatment is stated in this manner since there is no single routine technic applicable to all cases of cancer of the female pelvis. External irradiation with either 200 or 400 kv is a standard procedure in all stages of involvement.

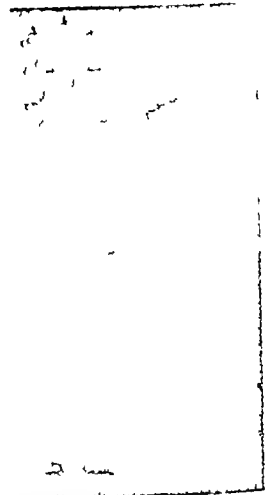


Fig 3 Roentgenogram of the female pelvis taken obliquely in the direction of the central beam for irradiation of the pelvis

unless it be the First Stage of cancer of the cervix. Since the First-Stage growths are so well localized, there are those radiologists who feel that either radium or intravaginal roentgen irradiation is adequate. Surgery also should cure 100 per cent of these cases. However, there is always a possibility that the cancer is not so limited to the cervix as it seems to be upon examination, and some of the cancer cells may have passed into the deeper lymphatics, and therefore external radiation may be advisable.

The ports for treatment by external radiation may be divided into two general

³ See Classification of the Cancer Committee of the League of Nations in Crossen H. S. and R. J. Operative Gynecology, St. Louis C. V. Mosby Co., 5th Ed., 1938. Also Schmitz Henry (1).

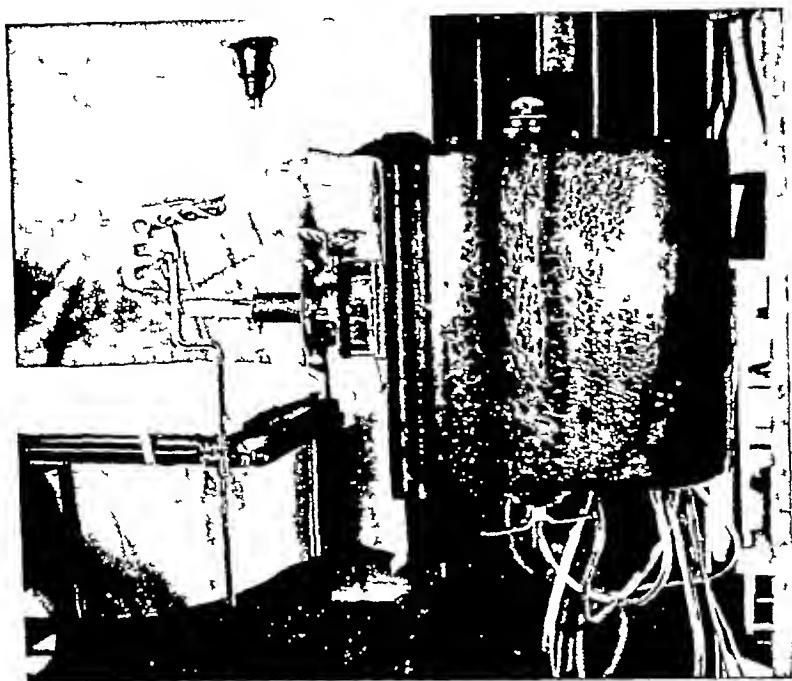


Fig 6 Apparatus for intravaginal roentgen therapy 200 kv

shown that a somewhat larger dose (approximately 1,000 r more) is necessary to produce necrosis of the intestine. One of the advantages of intravaginal roentgen therapy is that it offers a greater flexibility to deliver this remaining 1,500 r either into the cervix and uterus and broad ligaments or throughout the pelvis.

For intravaginal roentgen therapy, cones (Fig 6) are selected of a diameter suitable for the size of the vaginal canal, and multiple areas may be treated. These areas may be directed at the cervix and the surrounding structures or only at the cervix and broad ligaments. The radiologist must select the number of areas and dosage according to the case under treatment (either 140 or 200 kv may be used). Care must be exercised, however, in placing the cone so as to avoid overlapping of the areas and the production of a delayed reaction and a lack of uniformity of radiation about the uterus, the broad ligaments, and the lymphatic nodes along the lateral pelvic walls. If the vaginal canal will admit a fairly large cone, of 3 or 3.5 cm diameter

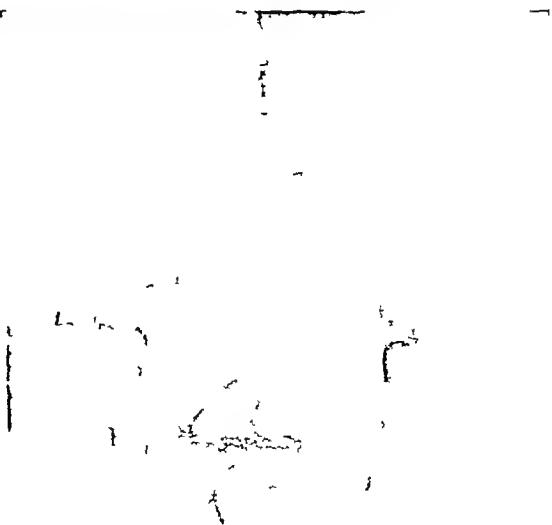
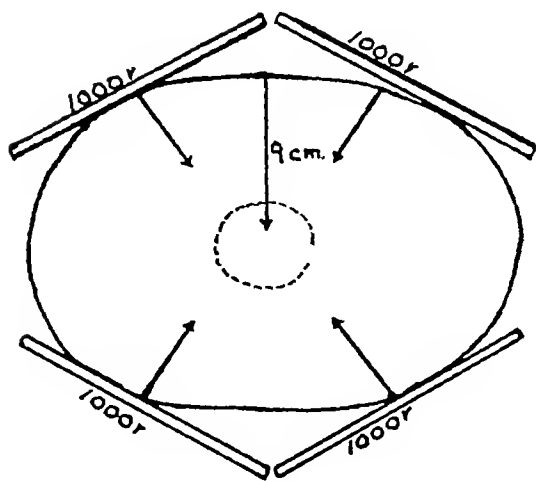


Fig 7 Roentgenogram of female pelvis with intravaginal cones in the vaginal canal with the central beam toward either ovary and the perimeter of the birth canal

(Fig 7), it is found that the radiation from it will cover the transverse diameter of the pelvis at the level of the uterus, provided three areas are given in the transverse

Tumor Depth and Dosage



*Total Tumor Dose From Five
External Areas - 400 KV \rightarrow 2500 r*

Fig 5 Diagram illustrating four oblique ports for irradiation of the female pelvis

classes In the first class, are those ports in which the ray is directed anteriorly or posteriorly with one port over each lateral pelvis and perhaps one over the perineum. The objection to this method is that a larger dosage of radiation must be applied to the skin in order to have adequate radiation throughout the pelvis. Very little depth dosage is obtained from lateral ports. In the other method of external irradiation, which may be called the cross-fire method, the ray is directed obliquely through the pelvis from both right and left sides and both anteriorly and posteriorly. To these ports is added one area over the perineum. If a roentgenogram (Fig 3) of the pelvis is made with the rays directed obliquely through the pelvis as just stated, it will be found that the birth canal and its anatomical structures are exposed to the radiation in all four positions. While this method permits some scattering of rays into the skin and superficial tissue of the side opposite the one being treated, and also a considerable exit dosage, the total radiation to the skin is considerably under that re-

quired for any permanent skin damage. It has been shown by Pendergrass and his co-workers (2) that skin damage can be expected in a significant percentage of cases where a dosage of 2,500 to 3,500 r as measured in air is given over a period of a few weeks. Such damage to the skin was the result of previous methods of treatment, in which only external irradiation was given and radium was placed within the uterus and cervical canal.

If the anatomical structures external to the birth canal were uniform in contour, then equal dosage could be given to any one of the four oblique areas with a resulting uniform dosage within the birth canal. Since this is not the case, measurements should be made obliquely through the pelvis in the line of the x-ray beam and the dosage computed according to the tissue intervening between the birth canal and the skin (Fig 4). If this is not done, then the areas of the anterior ports may transmit adequate dosage into the anterior portions of the birth canal while those lymphatic nodes lying deep in the posterior portions of the birth canal receive an inadequate dosage because of the depth of the buttocks. Such bad results occur with involvement of the lymphatic nodes in the lateral and posterior portions of the birth canal. This can be partially offset by use of a perineal port which brings these nodes, as well as the other female organs, more directly into the path of the roentgen rays.

In the average case, 2,500 r may be delivered into the structures of the birth canal by external irradiation without approaching the limit of skin tolerance (Fig 5). Also, this can be done so that the birth canal receives a rather uniform radiation. Since 4,000 r within the tumor cells is probably the optimal amount, there remain 1,500 r to be given either by intravaginal roentgen or radium therapy. Friedman (3) has demonstrated that a tissue dose of 4,500 r, delivered to the stomach over a period of approximately four weeks, will produce necrosis, ulceration, and, if the dose is 5,000 r or more, a large ulcer with occasional perforations. He has also

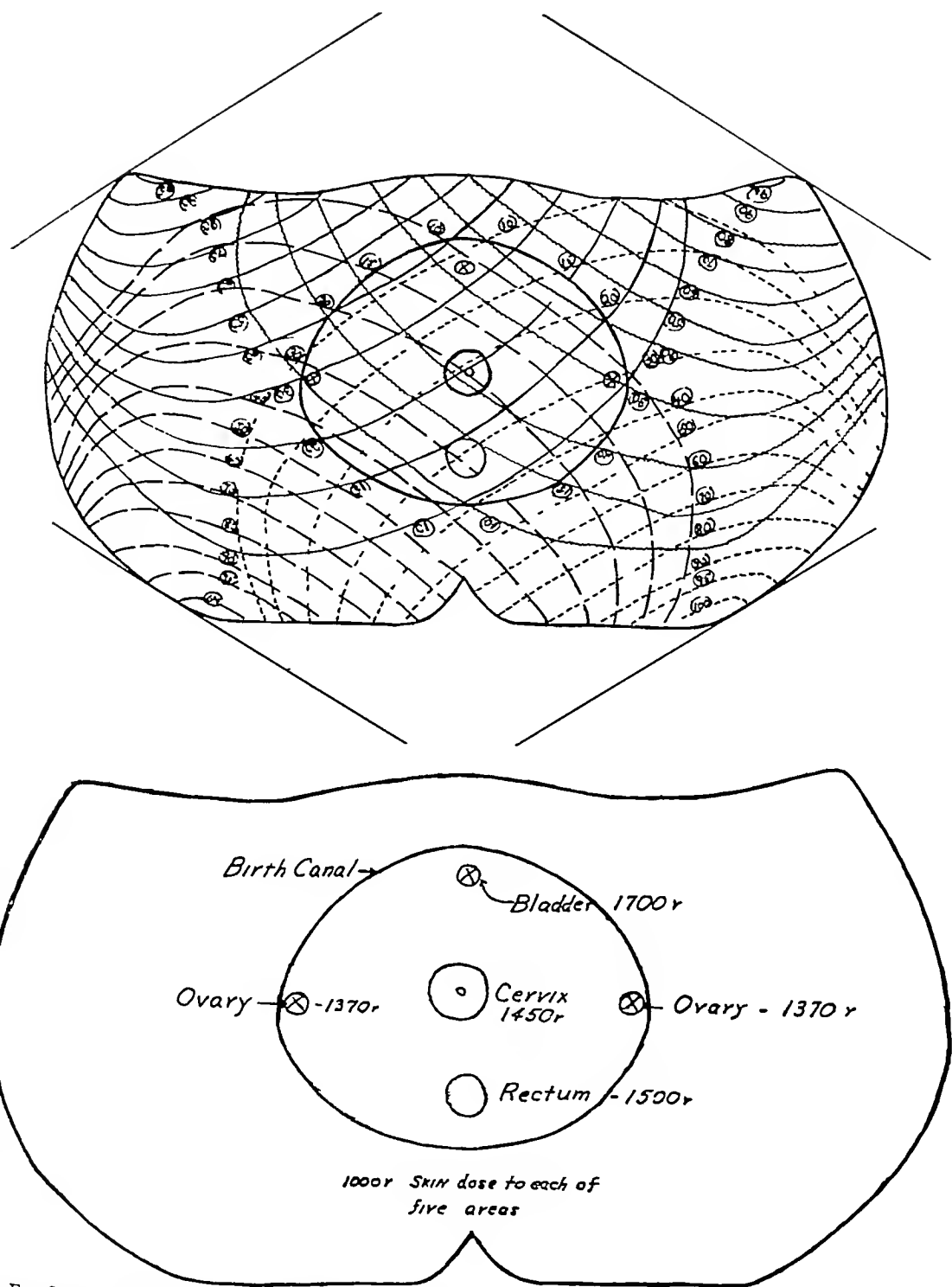


Fig 9 A Diagram showing computation of tissue depth dosage from four oblique ports, made by superimposing depth charts upon exact measurements of patient
 B Diagram of patient in A showing the tissue dose delivered into various portions of the birth canal from four oblique ports and one perineal port with 1 000 r measured in air given over each port

*Anterior Abdomen And Cone
Coverage of Pelvic Cavity*

*Pelvic Depth And
Cone Coverage*

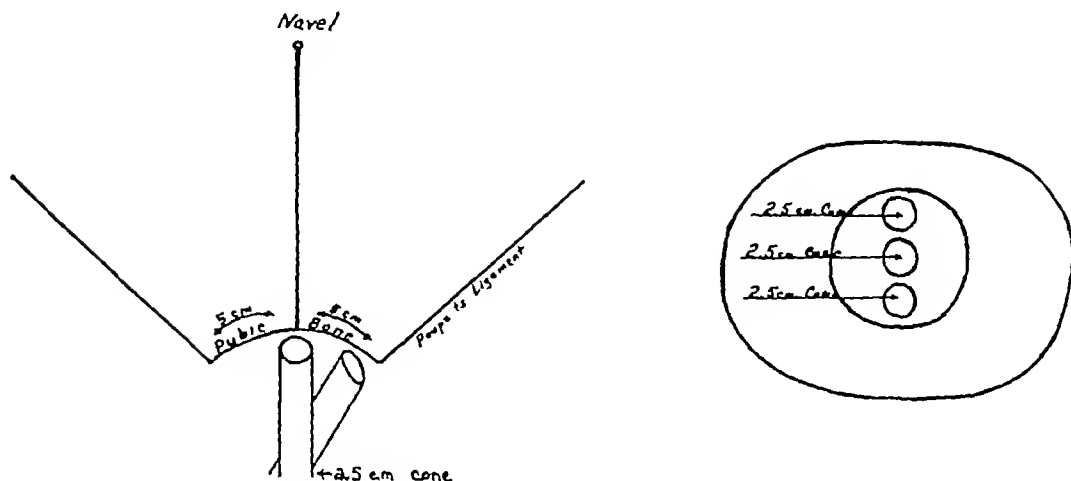


Fig 8 Diagrams illustrating inadequate coverage of the birth canal by small intravaginal cones

diameter, or it will cover the pelvis in the anteroposterior diameter if three areas are given in this diameter (4, 5). If a smaller cone is used, there will be a space between the areas treated which will receive very little radiation (Fig 8). The sum of the diameters of the areas treated must equal the diameter of the birth canal. In such a case, radium may be given within the uterus to complement the intravaginal roentgen radiation, and the intravaginal radiation should then be limited to the cervix and to the nodes along the outer pelvic wall since these nodes will not receive adequate radiation from the radium within the uterus. By this method, the additional 1,500 r may be supplied through the intravaginal ports and by radium within the uterus.

Radium should be used in the uterus and perhaps in the cervical canal in all Second, Third and Fourth-Stage cases to complement the external and intravaginal roentgen therapy. This is especially true when the intravaginal cone is not large enough, even with multiple ports, to deliver adequate dosage uniformly throughout the pelvic canal (Fig 9). In the early-stage, questionable cases in which there is a purulent discharge, radium should always be

used in the cervix and uterus. The radium dosage should be computed to complement the intravaginal and external roentgen therapy.

As stated in the introduction, it is not the purpose of this paper to quote statistics of brilliant results from the use of intravaginal roentgen therapy of the female pelvis, but rather to offer a method which seems a step nearer the production of uniform radiation of the birth canal, and to point out some of the obstacles which interfere with obtaining the best results. The authors have tried larger tumor doses than 4,000 r per series of treatments, and there was delayed reaction about two months following the second series in cases in which 5,000 r tumor doses had been administered in each series. Some of these delayed reactions about the cervix and vaginal vault healed with no permanent tissue damage, but an occasional patient was not so fortunate. Therefore, it is recommended that if a tumor dose of 5,000 r is given in one series, it should not be repeated, at least in that same amount. Further studies of this tumor dosage should be made. Also, it has been observed that there is an occasional failure if the cone used in the

con la selección de la técnica terapéutica. Debe dedicarse tiempo al estudio adecuado de cada caso.

En la mayoría de los casos, pueden llevarse 2,500 r a los tejidos del conducto genital por irradiación externa sin aproximarse al límite de la tolerancia cutánea. Para llegar a la dosis óptima de 4,000 r, pueden administrarse otros 1,500 r por vía vaginal con rayos X o con radio. La roentgenoterapia intravaginal posee la ventaja de que su mayor flexibilidad permite

llevar la dosis adicional bien al cuello y útero y ligamentos anchos o esparcirla en la pelvis. El número de zonas por tratar y las dosis respectivas tienen que ser determinados individualmente.

La roentgenoterapia intravaginal puede también utilizarse en los tumores residuales consecutivos a operaciones en el útero y ovarios y en el ciego, vejiga y recto. Menciónase la posibilidad de aplicar radio en el interior de la vejiga urinaria empleando un catéter modificado de retención.



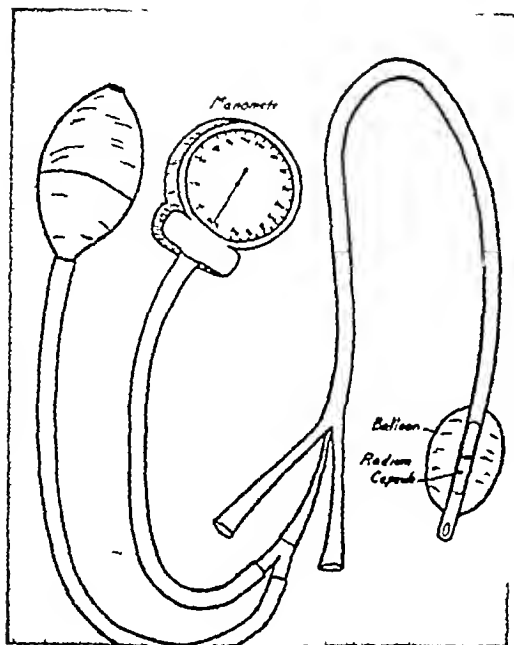


Fig 10 Diagram of retention catheter with radium capsule inside a balloon and a manometer attached for recording the degree of inflation of the balloon

external irradiation was not large enough to cover the lymph nodes along the lateral walls of the pelvis. With the use of intravaginal roentgen therapy there is a definite lack of damage to the skin because of the lower external radiation dosage, and less damage to the intestinal tract. The brilliant results, of course, are in the First, Second and some Third-Stage cases.

Intravaginal roentgen therapy has another application of considerable promise namely, for residual tumors following operations upon the uterus and ovaries, or about the cecum, bladder, and rectum. It is possible to cross-fire on these residual tumors through the vagina and by external irradiation, and to obtain results which have not been possible by other methods.

Also, the authors would like to offer another use of radium where an intracavity

application of it is desirable. By using a modified bladder retention catheter, the radium may be placed inside the catheter and inserted into the urinary bladder without difficulty. The balloon surrounding the radium is then inflated to the desired extent, and this degree of inflation may be recorded and controlled by a manometer (Fig 10). The inflation removes the radium from contact with the tissue under treatment and at the same time gives greater depth and uniformity of dosage, which has been sought for some time in the treatment of tumors of the bladder and other cavities. A limited use of this method has been quite satisfactory.

SUMMARY

- 1 The treatment of cancer of the female pelvis is a major procedure.
- 2 A careful diagnosis is absolutely necessary, as is a careful selection of the method of treatment.
- 3 There should be adequate time for study of each case.
- 4 Further observations with intravaginal roentgen therapy of carcinoma of the female pelvis are presented.
- 5 Another method for the application of intracavity radium irradiation is presented.

304 Republic Building
Denver 2, Colo

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SUMARIO

Roentgenoterapia Intravaginal del Cáncer de la Pelvis

El tratamiento del cáncer de la pelvis femenina representa un procedimiento de magnitud. Hay que mostrar el mayor cuidado en el diagnóstico y otro tanto sucede

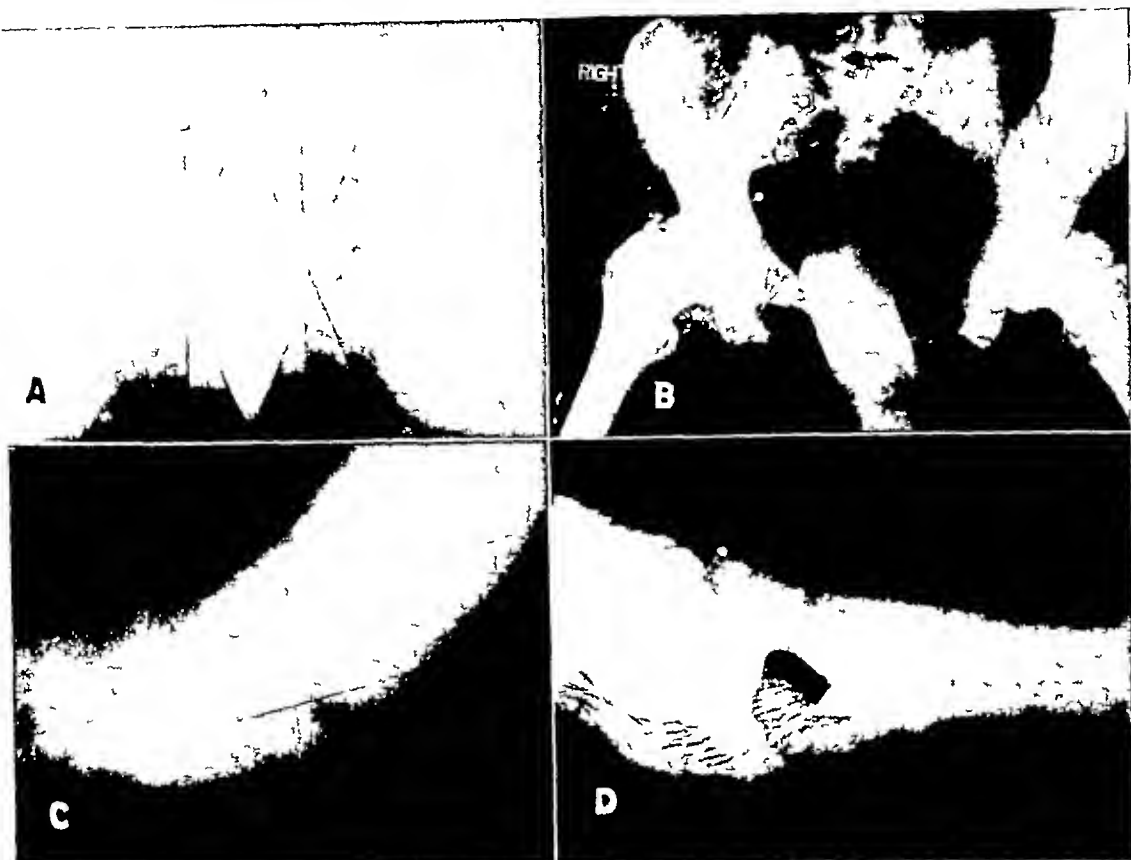


Fig 1 A Anteroposterior view showing pelvis of patient with 4-cm ϕ treatment cone in place in three positions (triple exposure) Lateral angulation of cones measured 30°

B Anteroposterior view of pelvis of cadaver with 4-cm ϕ treatment cone in place, angled 30° toward right side of pelvis Position of iliac and obturator nodes and lateral pelvic wall at level of internal os of uterus marked with lead shot

C Lateral view of pelvis of patient with 4-cm ϕ treatment cone in place, showing relation to promontory of segment

D Lateral view of pelvis of cadaver with 4-cm ϕ treatment cone in place showing relation to pelvic lymph nodes

using a radio-transparent cone (7) or by the use of an expanding speculum, as described by Erskine (2). The former may not be perfectly transparent, as the peripheral portions of the beam must pass obliquely through the length of the cone wall and not only through its thickness. The expanding speculum serves to decrease the danger of over-irradiating the bladder and rectum and yet allows for maximum spread of the beam. Some value has been attached, however, to irradiating the upper vaginal mucosa in order to attack the lymphatics in that area (11). In the calculations described here, all cones were taken to be 10 cm in length, they are indicated as radio-opaque or radio-transparent

Further deviation of the beam toward the parametria may be achieved by lateral angulation of the tube and cone with the patient in the lithotomy position. This has been described to an extent of 15 to 17 degrees (8), but greater angulation is possible (13). The smaller the diameter of the cone, the greater the angulation which can be achieved without discomfort to the patient. With a low- to medium-voltage machine, the tube head may be rotated to a vertical position and then angulated laterally to join the treatment cone without interfering with the patient's legs. Roentgenograms of patients with cones *in situ* have shown that a lateral angulation of 30° or more can be tolerated. Films have

Dosage Calculations for Various Plans of Intravaginal X-Ray Therapy¹

JAMES F. NOLAN, M.D., and WILLIAM STANBRO, M.D.

St. Louis, Mo

THE PROBLEM of achieving a wider and yet more uniform field of irradiation in the treatment of cervical carcinoma remains an important one. The necessity for this has been emphasized before (9). Briefly it can be stated that radiation treatment methods are limited by a maximum dose which can be delivered without causing dangerous necrosis and injury, while the effectiveness of a method depends upon a minimum dose which will be lethal to all tumor cells. In the treatment of cervical carcinoma these limitations become manifest in local slough and infection in the face of over-dosage, and in recurrence and metastases in the case of under-treatment. Because of these limitations, various methods have been adopted in the hope of solving the problem of uniform radiation. Examples of these are interstitial irradiation with needles and seeds, pneumoperitoneum with external therapy, treatment through external sciatic ports, and intravaginal cone therapy. The last named is considered here.

Intravaginal x-ray therapy has been advocated for many years by Merritt, Erskine, Morrison, Bouslog, Wasson, Sante, and others. This type of therapy offers the theoretical advantages of a uniform field, good dosage, and directional control (2, 3, 4). The preliminary effect of clearing up infection in fungating lesions, facilitating radium implantation at a later date, seems obviously important (7). Also the addition of appreciable quantities of radiation to the areas lateral to the cervix, which will be supplemented later by radiation from intracavity gamma-ray emitters, is advantageous (8, 13, 15).

This study has been undertaken to com-

pare different methods of intravaginal x-ray therapy on the basis of depth-dose calculations. Although the calculations made to accomplish these comparisons are entirely theoretical, practical considerations have limited the number of plans studied. The main treatment schemes for calculation and evaluation have been based upon experience with this type of therapy, as well as reports published by others (4, 7, 8, 11, 12, 13, 14). A discussion of the practical limitations of intravaginal therapy seems warranted here.

The larger the intravaginal port, the greater the divergence of the beam which is transmitted. A cone 4 cm in diameter is the largest size practical, but this may not be tolerated by all patients. With the use of lubricant and an obturator, however, it is possible in most cases to introduce a cone of 3 cm diameter without discomfort (13). Shortening the target-skin distance produces greater divergence of the beam. The use of a small tube head (as with the Phillips or Chaoul technic) which may be introduced into the vagina carries this to the maximum. Martius and Witte have achieved an almost "radium-like" local radiation field with a special tube head of this type (6). Such tubes, however, necessitate low voltages, which reduce the penetrability of the radiations. It has been found that about 30 cm is the shortest practical target-skin distance for the usual type of x-ray equipment used in intravaginal therapy (4). All the treatment schemes studied here have been on the basis of that distance.

Greater divergence of the beam may also be achieved by shortening the target-diaphragm distance. This can be done by

¹ From the Mallinckrodt Institute of Radiology and the Department of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, Mo. Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

TABLE II

Treatment Method								Calculated Radiation Distribution											
#	Plan Number	Quality of Radiation HVL	T.E.D. Value	Diameter of Cone Cm	Type of Cone Radio-opaque or Radio-transparent	Lateral Angulation of the Beam	Dose per Field (Air)	Total Dose per Plan (Air)	Level of Transverse Plane Through Pelvis	Dosage in "r" at Four Points in Pelvis				Deviation from Midline in "Cm" for Three Critical Isodose Levels					
										Midline	2Cm Lateral to Midline	4Cm Lateral to Midline	2Cm A.P. to Midline	Lateral			Antero-posterior		
														15 T.E.D.	7 T.E.D.	4 T.E.D.	15 T.E.D.	7 T.E.D.	4 T.E.D.
One Field	I	1mm Cu	700	4	T	0	8000	8000	Ext Os	9800	5400	3000	5400	0	2.75	3.5	0	2.75	3.5
									Int Os	7120	5000	2000	5000	0	2.25	3.5	0	2.25	3.5
	II	1mm Cu	700	4	T	0°	10000	10000	Ext Os	12000	8000	5000	8000	1	3.25	3.5	1	3.25	3.5
									Int Os	8900	6000	4000	6000	X	3.0	3.5	X	3.0	3.5
	III	1mm Cu	700	4	T	0°	12000	12000	Ext Os	14160	10500	6000	10500	2	3.25	3.5	2	3.25	3.5
									Int Os	10800	6100	5000	6100	X	3.75	3.5	X	3.75	3.5
	IV	1mm Cu	700	Oval 4 x 2	O	0	12000	12000	Ext Os	13200	9030	6000	2000	1.5	3.25	3.5	0.75	1.5	2.0
									Int Os	7200	5700	4000	3000	X	2.75	3.5	X	1.4	1.75
Two Fields	V	1mm AL	250	●	O	20 Rt	6000	12000	Ext Os	6900	5000	2000	3450	3.25	4.25	4.5	0.75	0.5	2.0
						20 Lt	6000		Int Os	1500	2000	1600	1000	X	3.75	4.75	X	X	1.5
	VI	4mm AL	300	●	O	20 Rt	6000	12000	Ext Os	7080	6000	2500	3540	3.0	4.5	5.0	0.75	2.15	2.5
						20 Lt	6000		Int Os	2100	3500	2500	1200	X	4.75	5.5	X	1.5	2.25
	VII	5mm Cu	500	4	O	20° Rt	6000	12000	Ext Os	7200	6800	3000	3600	0	4.25	4.5	0	2.0	2.25
						20 Lt	6000		Int. Os	2300	4500	3500	1500	0	4.0	5.0	0	X	0.5
	VIII	5mm Cu	500	3	T	30 Rt	6000	12000	Ext Os	6900	6000	2800	3450	0	3.5	4.75	0	2.25	2.5
						30 Lt	6000		Int Os	4920	4100	3000	2800	0	3.25	5.0	0	1.5	2.5
Three Fields	IX	5mm Cu	500	3	O	0	4000	12000	Ext Os	13600	5000	1000	0	1.5	2.25	3.25	1.25	1.5	2.0
						30° Rt	4000		Int Os	5000	4000	1500	1000	X	2.25	3.5	X	1.25	1.5
						30° Lt	4000												
	X	5mm Cu	500	4	O	0	4000	12000	Ext Os	4800	4700	3500	3500	0	3.75	4.25	0	2.0	2.5
						30° Rt	4000		Int Os	3480	2000	2500	2000	0	X	5.0	0	X	2.25
	30° Lt	4000																	
	XI	5mm Cu	500	4	O	0	4000	12000	Ext Os	4800	4350	2500	3500	0	3.5	4.0	0	2.0	2.5
						30° Rt	4000		Int Os	3500	3500	2500	2000	0	2.0	3.75	0	0.5	2.0
30° Lt	4000																		
XII	5mm Cu	500	4	O	0	4000	16000	Ext Os	4800	7500	3500	3500	0	4.25	4.5	0	2.0	2.5	
					30° Rt	6000		Int Os	3500	4500	3500	2000	0	4.25	5.0	0	0.5	2.0	
30° Lt	6000																		

NOTE X indicates that the isodose line in question does not extend to the depth of the internal os

These showed good correlation for the three sets of data at the center of the beam, but for the peripheral regions the calculated dose was lower than the measured dose. The depth-dose data used are presented in Table I

also been used to study the relation of commonly involved lymph nodes to intravaginal beams of radiation. The positions of the obturator and hypogastric nodes and the lateral pelvic wall were marked with lead shot in a cadaver. Cones of various diameter were placed in the vagina and angled to 30 degrees in the horizontal plane. Roentgenograms of the pelvis made in the anteroposterior diameter show that a con-

for their evaluation and comparison. The calculations were derived from published depth-dose tables (5,10). It is extremely difficult to obtain accurate depth dose data experimentally with small fields of irradiation. That is because the usual instrument for measurement—the ionization chamber—must necessarily occupy some space, and the actual diameter of the chamber may represent a large percentage of the

TABLE I
Calculated Depth Doses for Center of the Beam
Given in Percentage of Air Dose

Quality of Radiation		HVL - 1mm AL			HVL 4mm AL			HVL 5mm Cu			HVL 1 mm Cu		
Factors	KV	100			120			140			200		
Filter		0			1.0 mm AL			0.25 mm Cu			0.5 mm Cu		
TSD		30 Cm			30 Cm			30 Cm			30 Cm		
Cone Diameter (Cm)		2	3	4	2	3	4	2	3	4	2	3	4
Depth (Cm.)	0	105%	112%	115%	108%	115%	118%	110%	115%	120%	110%	115%	120%
	1	50	60	64	78	87	92	93	100	105	100	105	105
	2	34	40	43	56	64	72	76	82	87	84	85	89
	3	22	26	30	44	50	55	64	68	71	70	71	76
	4	16	19	21	33	39	44	49	52	54	56	59	63
	5	11	13	15	25	30	34	39	44	45	44	45	52
	6	8	10	11	18	23	26	33	37	38	36	37	44
	7	6	7	8	14	18	20	25	28	30	30	32	36
	8	5	5	6	12	14	16	21	25	27	24	26	30

siderable degree of angulation is necessary for the nodes to be included within the beam.

Lateral roentgenograms reveal that it is necessary to depress the perineum and aim the cone upward. This may not be possible in every instance, but the attempt should always be made to direct the beam out of the hollow of the sacrum to avoid direct irradiation of the rectum.

Various theoretical treatment plans were laid out and dosage calculations were made

diameter of the field being explored. Measurements in the center of small beams are probably quite accurate, but those in the periphery may be inaccurate. In the present calculations, the depth dose at the periphery of the beam was considered to be one-half of the dose at the center of the beam at the same depth (10). One radiation scheme used was compared with similar ones for which measurements were made by Morrison (8) in a rice phantom and by Erskine (2) in a water phantom.

RADIATION DISTRIBUTION
THROUGHOUT PELVIS
FOR
INTRAVAGINAL TREATMENT

Plan VII

Cm

Factors 140 KV 25 mm Cu 30Cm TSD

Cone 4 Cm.D Opaque

Field A - 20 Angulation - Dose 50%

B 20 Angulation - Dose - 50%

Isodose lines in per cent of total air dose

Fig 3

RADIATION DISTRIBUTION
THROUGHOUT PELVIS
FOR
INTRAVAGINAL TREATMENT

Plan XII

Cm

Factors 140 KV 25 mm Cu 30 Cm TSD

Cone A 3Cm.D Opaque

B 4Cm.D Opaque

C 3Cm.D - Opaque

Field A 30° Angulation Dose 37.5%

B 0 Angulation Dose 25 %

C 30 Angulation Dose 37.5%

Isodose lines in per cent of total air dose

Fig 4

With these values, twelve treatment schemes were explored. Diagrams were made to represent a uterus of normal size in standard relationships to the pelvic walls and adjacent viscera (1). On these, the radiation fields were laid off to scale, and calculations were made to determine the amount of radiation which would fall at certain points throughout the pelvis.

of cones, or use of radio-transparent cones, changes in the direction of the beam of radiation, and the dose applied per field, as well as the total vaginal dose for each method.

In order to compare the various plans, the right side of Table II gives the distribution of calculated doses of radiation. Two different transverse levels were chosen for

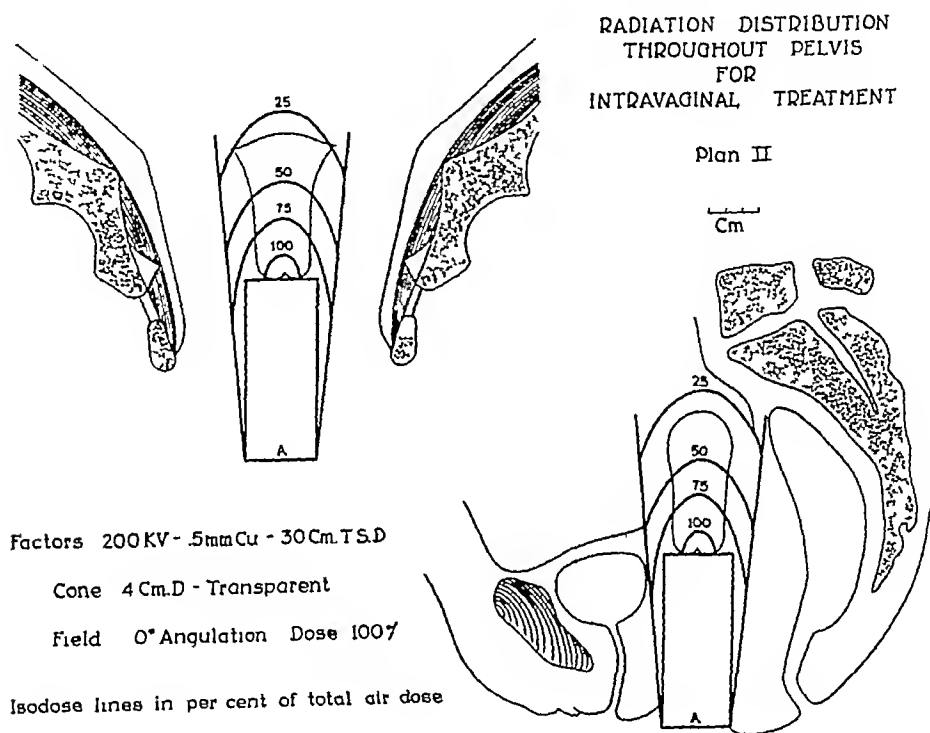


Fig 2

Figures 2, 3, and 4 show the distribution of radiation throughout the pelvis for treatment Plans II, VII, and XII. These are drawn so that the isodose lines represent percentages of the total dose (measured in air) delivered at the vagina by each scheme. Diagrams of this type were drawn for each of the plans studied, and from these the pertinent data were derived for comparison of the methods. The left side of Table II shows variations in the method of treatment for one-, two-, and three-field techniques. The variations include changes in quality (half-value layer), alterations in size of field as determined by the internal diameter

of these calculations. One of these is that of the external os. The other is a transverse plane through the internal os. The number of roentgens reaching the mid-line is shown for each of the two planes in question. Other additional points were selected for calculations. Two of these are lateral to the mid-line and one is in the anterior-posterior direction. Finally, certain critical isodose levels were selected and expressed in terms of threshold doses. The distances lateral to or anterior and posterior to the mid-line, at which those amounts of radiation fell, are given in centimeters for each of the two planes considered.

r is too much for the softer types of radiations, as fairly wide areas of probable necrosis are indicated. However, radiation of 0.5 mm Cu h v 1 (140 kv, 25 mm Cu filter) yields no area of necrosis because of its higher value per T E D.

The fourth scheme in this group utilizes a smaller cone (3 cm diameter), of trans-

3 cm diameter with the lateral ones angulated at the mid-point of the cervix. Plan X utilizes a large central cone (4 cm diameter) with the lateral ones, of only 2 cm diameter, placed in the fornices and angulated at the lateral edge of the cervix. Plan XI uses a large central cone 4 cm in diameter, with two lateral cones 3 cm in diame-

Graph Showing Radiation Distribution for Three Intravaginal X-ray Treatment Plans at Transverse Plane Through Pelvis at Level of Internal Os

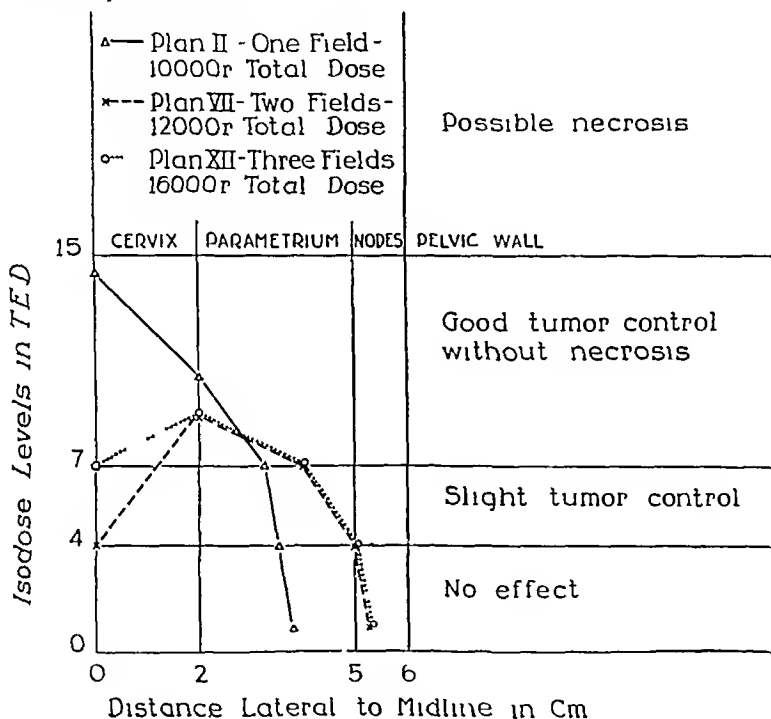


Fig 5

parent type, and a wider angulation (30° instead of 20°). The quality of radiation is the same as in Plan III. With this plan the amount of radiation is not so great at the points indicated as with the larger opaque cone angulated to a lesser degree.

The third section of Table II presents the data from four plans of treatment which utilize one straight cone and two angulated ones (13). For the first three, the quality, dose, and angulation are kept constant, but the size and position of the cones are varied. Plan IX calls for three cones of

ter angulated at a position 1 cm lateral to the external os. Studying the table, one sees that the overlapping of Plan IX may be dangerous and that the spreading out of the cones, as in Plan X, does not yield very effective radiation at the level of the internal os. Plan XII is essentially the same as Plan XI except that the dose delivered by each lateral cone is increased to 6,000 r (or 37.5 per cent of the total) and that the central cone remains at 4,000 r (25 per cent of the total). Even with this increase, there will probably be no necrosis,

The transverse planes through the pelvis shown are those at the level of the external os and the internal os. The former is important because it represents the plane of limitation for intravaginal treatment methods. That is, the dosages delivered cannot be carried above those which may cause necrosis here. The plane through the internal os is important because it represents the effective plane. Here carcinoma of the cervix most often spreads laterally by direct extension or through lymphatics. The dosages delivered here should be kept below those which might cause necrosis and yet lie in the range that will control tumor cells.

Because of the fact that threshold erythema doses represent rather extensive assumptions so far as biological reaction is concerned (16), the actual roentgens at certain points in the pelvis are presented. These exclude any variability of biological reaction with quality of radiation, but are accurate for comparing radiation schemes of the same quality. The points taken are those at the mid-line, 2 cm lateral and 2 cm anteroposterior to the mid-line, and 4 cm lateral to the mid-line. These four points in the two planes indicated represent the areas most important in this type of therapy.

The critical isodose levels chosen are those of 15, 7, and 4 threshold erythema doses. These are considered as being indicative of definite biological reactions (1). Doses of 15 T E D or above may cause tissue necrosis and detrimental effects. Doses from 7 to 15 T E D are adequate for tumor control without causing necrosis of normal tissue. Doses of 4 to 7 T E D are less than adequate, but are important because they may reinforce radiation delivered through other treatment ports.

The first section of Table II describes four treatment plans which utilize one field centered on the cervix. For these, a quality of radiation which would yield good penetration was assumed and a transparent cone of the largest possible diameter was simulated. The first three plans were prepared to show the effect of variation of

dose, and the fourth was calculated to find the effect of a shaped cone.

From the table one can see that, as dose is increased, the depth dose also increases. Treatment schemes for such a method have been used and advocated for a total of from 7,000 to 8,000 r (air) (8). Plan I represents this scheme at 8,000 r, no necrosing dosages appear, but the depth dose lateral to the internal os is not great. Plan II, for which 10,000 r (air) is calculated, shows a small area of possible necrosis but probably could be used. Because of the area of probable necrosis in Plan III, in which 12,000 r (air) is simulated, it would be unwise to carry the dosage thus far if the assumptions made as to predicted biological reaction are correct. Plan IV shows the results from an oval cone (4×2 cm) with the dose carried to 12,000 r. Such a plan might protect the area of the vesicovaginal and rectovaginal septa and yet allow lateral spread of the beam (4). The cone simulated is opaque. The figures indicate that this plan yields about the same results as Plan II (a circular cone for 10,000 r) lateral to the mid-line and appreciably less in the anteroposterior direction. From these data, we may conclude that such one field treatment plans with circular transparent cones are limited to a dosage level of 8,000 to 10,000 r in air and that the area of effective radiation extends for about 3 cm from the mid-line at the level of the internal os.

The second section of Table II is presented to show the effects when the higher-voltage radiations are sacrificed to achieve a greater angulation of the beam by lateral direction of the cone (13, 15). The first three schemes utilize an opaque cone of 4 cm diameter, with an angulation of 20 degrees in the horizontal plane. Different qualities of x-rays are compared, the total dose delivered being kept at 12,000 r or 6,000 r per field. As the quality of radiation is increased, the penetrability is also increased, so that the dose reaching the deeper tissues becomes greater. If we consider it possible to translate the roentgens delivered into T E D, we find that 12,000

be delivered to tumors through the intravaginal ports. The addition of this method to one's armamentarium permits greater individualization of treatment methods. From such procedures an improvement in clinical results is to be expected.

SUMMARY

1 The distributions of radiation for twelve practical plans of intravaginal x-ray therapy were calculated from published depth-dose data.

2 The effects of variation in size, shape, type, direction, and combination of cones were studied.

3 The variations in radiation distribution were evaluated upon the basis of roentgens delivered to certain points in the pelvis and also upon the basis of expected biological response.

4 Conclusions are drawn from these studies that intravaginal cone therapy may well be a useful tool in the treatment of carcinoma of the cervix. Within its limitations it can be expected to contribute to better results in the treatment of cervical cancer by irradiation methods.

ACKNOWLEDGMENT The authors wish to express their appreciation to Dr E H Quimby of the College of Physicians and Surgeons, Columbia University, New York City, for her generous aid and advice in the determination of the basic depth-dose values used in this study. They also wish to thank Miss Elizabeth Ley of the Mallinckrodt Institute of Radiology, Washington University, St Louis, Mo, for the preparation of the diagrams and tables.

630 S Kingshighway Blvd
St Louis 10, Mo

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DISCUSSION

(Papers by W W Wasson and J F Nolan and Wm Stanbro)

Arthur W Erskine, M D (Cedar Rapids, Iowa) It has now been demonstrated theoretically, experimentally, and clinically that the most effective means of destroying the primary tumor in cancer of the cervix is by the direct application of x-rays (the so called transvaginal or intravaginal method). The chief objection to the method is the difficulty of exposing a sufficiently large field. The great advantage of the multiple-field method is that a large area can be exposed through a small introitus. For example, if the introitus will only admit a speculum with a circumference of 12 cm, it is possible to expose a total area 7.5 cm by 6.4 cm, as shown in Figure 1. (This is not the way Dr Wasson does it, but it could be done this way and I selected this position of the five fields since they expose a rectangular field, which is desirable because it ensures adequate dosage to the lateral vaginal fornices, and since they show maximum overlapping.) This is a much larger field than can be adequately exposed by any other method through such a small introitus.

An objection which might be made to the use of overlapping fields is that they produce inequality of distribution. In order to talk intelligently about this I had some measurements made with the chamber at the points A, B, C, D, and E, as indicated on Figure 1. The results are shown in Tables I and II. For Table I the chamber was barely submerged. For Table II it was

and this redistribution of the doses yields a much more effective spread of radiation at the level of the internal os

In order to compare the one-, two-, and three-field schemes which could be used without danger according to these calculations, Figure 5 was prepared. This graph indicates various isodose levels and their possible biological effect on one co-ordinate and the position of those isodoses lateral to the mid-line at the level of the internal os on the other co-ordinate. Plan II, which is a one-field scheme carried to 10,000 r, shows no necrosis in the cervix at the level of the internal os, but a sharp fall in the amount of radiation in the area of the parametrium. Plan XII, which is a three-field method carried to 16,000 r, increases the effective radiation in the cervix itself but maintains the lateral spread of Plan VII.

One must be careful in drawing conclusions from a work of this sort that is based entirely on calculations, which admittedly may not be basically absolute. We must reiterate that the factors taken to translate the calculated figures into a common denominator, which would indicate expected biological reaction, may be inexact. Furthermore, the stylized treatment plans considered here could hardly be duplicated under actual treatment conditions in all patients. Distortion and fixation of the vaginal walls may interfere with insertion of vaginal cones. If, however, one considers the shape of the radiation distribution curves which have been prepared for these comparisons, and not the numerical results, one finds that certain concepts are borne out. These concepts are important in the consideration of this type of therapy from a clinical point of view. These may be discussed as follows.

(1) The one-field treatment plan with optimum physical factors is limited, so far as dosage is concerned, by the reaction at the level of the external os, which represents the portal of entry. The field of radiation is essentially similar to that from an intracervical tandem plus colpostat arrangement for radium. Such a one-field treatment method does not provide enough

energy to the lateral parametria to control growing cancer cells even when the amount of radiation delivered at the portal of entry is carried to its maximum. The method could well be used, however, at a lower dosage as a preliminary to radium implantation. This would bring about the effects of primary regression and control of infection mentioned before. In cases of carcinoma of the cervical stump, where radium implantation is difficult, this method would perhaps provide a better field of radiation.

(2) The two-field method of irradiation is obviously inadequate for the control of tumor cells confined to the cervix itself. If, however, one considers the isodose shape for such a treatment method, and those for a combination of intracervical tandem and interstitial needles (9), one is struck by the idea that they would well complement one another. The facts that the intravaginal cones contribute their greatest dose at the vaginal mucosa, and the long radium sources contribute theirs at the mid portion of their lengths, result in a spatial separation of the portals of entry or limiting points so far as maximum dose is concerned. It is quite conceivable that, with a combination of these two types of therapy, the energy delivered by each could be kept below the level that would cause dangerous necrosis, and yet more effective radiation would be delivered throughout the pelvis than with one of the methods alone. Since the energies of the x-rays considered in the present calculations are so different from gamma radiations, no attempt has been made here to predict the biological reactions which would result from such a combined treatment method.

(3) The radiation distribution for the three-field method of treatment would seem to be as effective as that obtained from intracavitary or interstitial radium applications. Intravaginal roentgen treatment carried to its maximum limit could be used without radium.

(4) The most promising concept that this study teaches us is that considerable variations of treatment methods are possible, and effective amounts of energy may

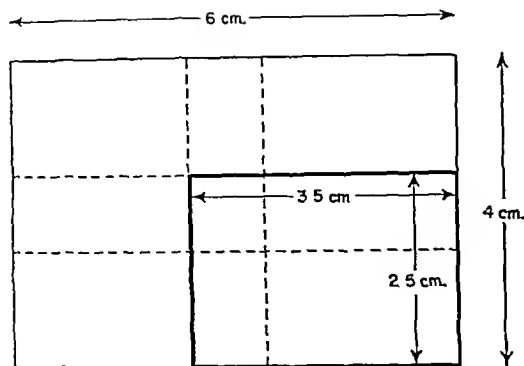


Fig 3 Diagram showing four overlapping rectangular fields

It is apparent that there is now a great deal of interest in the transvaginal method and that many, perhaps most, of you will soon be using it. Those of us who have been using one or another modification of the method for several years would indeed be remiss in our duty if we failed to point out *now* some of the pitfalls that have beset us and to urge you to control your initial enthusiasm, to make complete examinations and careful classifications, to keep decent records, and above all to avoid the dangers of over-dosage, which, as Dr Wasson has pointed out, are real.

Finally, this rather elementary study of scattering and distribution of the x-rays used in a technic something like the one used by Dr Wasson justifies the following conclusions:

1. The distribution over the entire combined field both at the surface and at a depth of 3 cm is nearly enough uniform, and is especially good at the edges of a rectangular field.

2. The depth dose percentage at 3 cm is higher than it needs to be.

3. Softer rays produced by lowering the voltage, or preferably by using less filter, would be better (theoretically).

4. Diminishing the depth-dose percentage by shortening the anode skin distance as well as using softer rays would, theoretically at least, improve the method.

5. The possibilities of exposing four adjacent rectangular fields should be explored first by laboratory experimentation, and, if the results justify it clinically.

Axel N Arneson, M D (St. Louis, Mo)
From the program at this meeting, as well as from private discussions, it is evident that there is great interest in intravaginal treatment with x-rays. That interest has been stimulated by Dr Wasson, Dr Erskine and many others. It has been my good fortune several times to discuss with Dr Nolan the problems in his paper. At the outset it may appear that he has presented complicated data. He has used complicated data to explore different possibilities for intravaginal x-rays.

The result has been a contribution toward simplifying procedures that can be used.

The usefulness of intravaginal x-rays can best be shown on the basis of clinical results. To be sure, the amounts applied intravaginally must be correlated and integrated with x-rays administered externally, and with radium applied to the cervix and uterus. We have in intravaginal x-ray therapy an added tool for increasing materially the amount of radiation falling upon the cervix itself. The rate of administration can be varied over a wide latitude. It has been pointed out that we may expect better regression and more favorable control of infection. It is also obvious that intravaginal x-rays can be used to increase the effective radiation throughout the tumor-bearing region.

Mention should also be made of additional uses for intravaginal x-rays. Various types of lesions occur within the vagina. Some are primary, and others are metastatic from cervical or from corpus cancer.

Both essayists are to be congratulated. It is wholesome to see work directed toward exploring different possibilities for this method of treatment.

Dr H J Ullmann, M D (Santa Barbara, Calif.) I would like to ask Dr Nolan, first, if this 16,000 r is the tissue dose in the region of the cervix or parametrium. I want to get it clear whether he referred to the surface dose of all ports added together or whether he referred to a true tissue dose. I also want to inquire, whether, where this dose has been given, he adds radium. I am not sure that I heard whether or not this was done.

I want to add one point to the discussion, and I feel very strongly about it. It is that no one should gain the impression from these papers that cancer of the cervix can be treated at a kilovoltage of 140 or less. One should not treat cancer of the cervix with equipment limited to less than 200 kilovolts. For portions of the treatment where 140 kv is indicated, this is available with the same machine, but one should not be limited to 140.

Harry H Bowling, M D (Rochester, Minn.) My chief interest in this technic concerns the adequate treatment of the involved peripheral lymph nodes in cases of carcinoma of the cervix. For example, the primary lesion of an average stage 3 carcinoma of the cervix can be rather promptly controlled by intracavitary radium therapy and supplemental roentgen therapy, however, the control of the involved peripheral lymph nodes remains a problem for the therapeutic radiologist. The various methods of intravaginal roentgen therapy may furnish an additional port of entry for roentgen rays and thus increase the total depth dose.

I hope these workers will extend their interest in obtaining, if they can, an increased depth dose in the fields of peripheral node involvement.

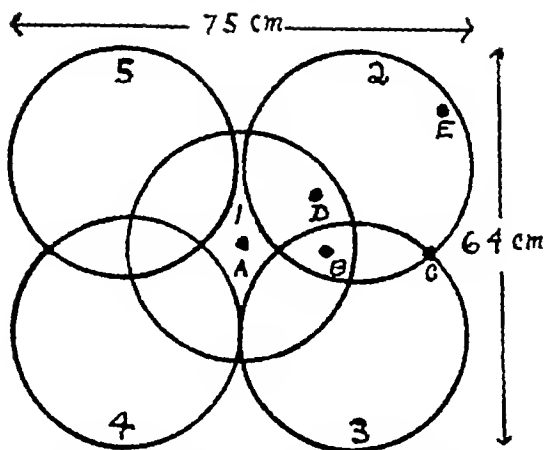


Fig 1 Diagram showing size of total field exposed by five overlapping fields 3.75 cm in diameter. Letters indicate points at which tissue dose was measured.

TABLE I TISSUE DOSE AT SURFACE PER 100 R (measured in air) TO EACH OF FIVE FIELDS*

Position of Chamber	1	2	3	4	5	Total
A	118.0	31.5	31.5	31.5	31.5	244.0
B	106.0	106.0	106.0	19.5	19.5	357.0
C	39.0	98.5	98.5	19.5	19.5	275.0
D	110.0	110.0	31.5	19.5	19.5	280.5
E	39.0	110.0	31.5	19.5	19.5	219.5

* 200 kv, 35 cm ASD filter 0.5 mm Cu h.v. 1.09 mm Cu diameter of circular fields 3.75 cm

submerged to a distance of 3 cm. In both cases 100 r as measured in air was given to each of the five fields without moving the chamber. The following factors were used: 200 kv, 20 ma, copper filter 0.5 mm, 35 cm anode skin distance, h.v. 1.09 mm copper, diameter of circular fields 3.75 cm.

In Table I you might expect point B to receive three times the dose received at point A, because it lies within the circumference of three fields. What actually happens, as shown on the first line of the table, is that the 100 r given to point A (measured in air) is increased by back scatter to 118, but point A also receives about 31 r from each of the surrounding fields so that the total tissue dose to point A is 244 r. Point B receives 106 r from each of the fields 1, 2 and 3, but only 19.5 r by scattering from fields 4 and 5 so that the total is only 357 r. The differential between the maximum and minimum dose received at any part of the surface is small (the ratio being about three to two). The reasons are scattering and the fact that the dose at the edge of the field is much smaller than it is in the center because of the excessive diaphragming.

TABLE II TISSUE DOSE AT 3 CM DEPTH PER 100 R (measured in air) TO EACH OF FIVE FIELDS*

Position of Chamber	1	2	3	4	5	Total
A	86.5	43.5	43.5	43.5	43.5	260.5
B	71.0	71.0	71.0	23.5	23.5	260.0
C	62.0	79.0	79.0	15.5	15.5	251.0
D	86.5	86.5	19.5	15.5	19.5	227.5
E	62.0	79.0	31.0	15.5	31.0	218.5

* 200 kv, 35 cm ASD filter 0.5 mm Cu, h.v. 1.09 mm Cu, diameter of circular fields 3.75 cm

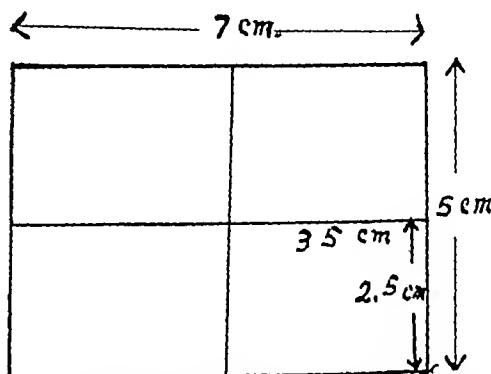


Fig 2 Diagram showing four adjacent rectangular fields.

Table II shows a surprisingly large total depth dose percentage because scattering is at a maximum at a depth of 3 cm, with this hardness. The surface dose at point C, which is just at the edge of the fields at the surface is 275 r, but the depth dose is 251 r because, due to the divergence of the beams, the point then lies well within the circumference of the two beams. The large depth dose undoubtedly explains the frequency of proctitis. It might be better to use somewhat softer rays, possibly with a h.v. of about 0.5 mm copper, this hardness produces maximum back-scatter.

It is now possible to obtain tubing of any required shape for the periscopic intracavitary cone. I suggest that somebody try experimentally four oblong fields. If the introitus will only admit a speculum with a circumference of 12 cm, one could use a rectangular tube 2.5 x 3.5 cm. If four fields could be accurately exposed, as shown in Figure 2 it would be possible to treat a total field 5 x 7 cm. There would of course be some danger of overlapping the four fields, as shown in Figure 3, which would produce an overexposure of the central centimeter but with care and the use of the periscope this danger would be minimized. Even though the fields were overlapped so that the central centimeter received four exposures the ratio between the maximum and minimum dose would not be more than two to one.

cervical radium. Clinically it would be unwise to depend on this or any other single treatment method, since results from a combination of treatment methods are usually superior in a wider range of patients. We have made no brief for the exclusion of other treatment methods in favor of intravaginal x rays, although in some clinics

external and intravaginal x-rays are advocated instead of external x-rays and intracavity radium. In our own experience we have found that intravaginal x-rays may be combined with other methods of treatment (external x-rays plus intracervical and parametrial radium) to yield impressive preliminary results.

SUMARIO

Calculo de la Dosis en la Roentgenoterapia Intravaginal

Tomando los datos publicados acerca de profundidad-dosis se calculó la distribución de la irradiación con doce planes factibles de roentgenoterapia intravaginal, con uno, dos y tres campos.

Estudiáronse los efectos de la variación en tamaño, forma, tipo, dirección y combinación de conos.

Avaluáronse las variaciones en la distribución de la radiación, tomando por base los roentgens entregados en ciertos puntos

de la pelvis y también la respuesta biológica esperada.

El concepto derivado de este estudio que más promete es que es posible introducir considerables variaciones en las técnicas terapéuticas, y que pueden llevarse a los tumores dosis efectivas de energía por vías intravaginales. La adición de esta técnica al arsenal disponible permite una individualización mayor del tratamiento y debe conducir a un mejoramiento de los resultados clínicos.



J A del Regato, M D (Columbia, Mo) I am glad to be able to participate in the discussion of this very important subject. I would like to point out that the dosage calculations of Drs Nolan and Stanbro are based on consideration of transvaginal roentgen therapy alone. They have shown that with the use of a large speculum the irradiation is greater in the mid-line and that it rapidly decreases toward the wall. This would imply a condemnation of the use of this type of transvaginal roentgen therapy in favor of the use of smaller metal cylinders directed to cover alternately both sides of the pelvis and the cervix.

One can, of course, irradiate the parametria and even the pelvic wall with the use of a narrow transvaginal beam, but the argument is that such approach would not achieve a homogeneous irradiation of the diseased area, nor a sufficient one. One cannot accurately include an entire carcinomatous parametrium in a narrow beam of radiation 3 cm in diameter. We consider this a futile attempt without precision.

The success of radiotherapy of cancer depends on the ability to distribute a necessary minimum of radiations as homogeneously as possible throughout the tumor area in order to diminish the untoward effects on the normal structures. In the treatment of carcinoma of the cervix, this cannot be accomplished with external irradiation alone (with 200 kv), and an internal treatment is necessary as a complementary phase. Hence, transvaginal roentgen therapy should be used to assure its best possible adaptation to the external pelvic irradiation. We think that this is best accomplished with the use of a large speculum with transparent walls. We have treated over 200 consecutive cases of carcinoma of the cervix by transvaginal roentgen therapy following external irradiation, in no case was it necessary to use a speculum less than 3.6 cm in diameter. Our field opens to a circle 6 cm in diameter at the level of the cervix and consequently assures irradiation of fornices and part of the parametria, our speculum provides protection for the vulva and also for the bladder and rectum, if it is indicated.

I would like to congratulate Drs Nolan and Stanbro on their serious attempt to evaluate the different methods of transvaginal roentgen therapy, but I would like to re-emphasize that any such attempt would have to consider their value in association with the external irradiation of which they are intended to be a complement.

Dr Wasson (closing) I wish to thank the discussants, and to express my appreciation of Dr Nolan's calculations and those of Dr Erskine. The final technic which ultimately will be worked out will result from the investigations of such men as Dr Nolan and Dr Erskine.

What I presented to you were clinical observations, and I said nothing about results. I do want

to stress certain points very briefly. First, in regard to diagnosis, and second, selection of method. Let us not distort our perspective so that we see only one method of treatment, it may be surgery, it may be radium, it may be intravaginal x-rays, or it may be a combination of all of them.

Now just a word with regard to the radiation dosage. The interest shown here creates in my mind a little fear that we may overdo the dosage of radiation, and that we may throw disrepute on a fairly good method, for I have found that it is easy to get an over dosage by the intravaginal method. The r's, you know, slip in there so easily that it is astonishing. And I have had delayed results, I have had delayed necrosis some two months after the second series. I have found that when we go to a 5,000 or 6,000 r tumor dose—I repeat, *tumor dose*—then it is wise to be careful about its repetition—*very careful* about its repetition. Again, in regard to tumor dose, we should calculate the dosage from each cone and not add the r output from all the cones together and consider that the tumor dose.

Today, apparatus is becoming more readily available to us, and one of these days, I think, we will have tubes that will give us a greater r output, so we will be able to give this treatment adequately and rather quickly.

Dr Nolan (closing) There have been several questions raised which have to do with the relationship of the calculations performed and their clinical application. Such questions as, "Why were simulated doses presented for total plans of treatment rather than for each field (as is the more accurate and accepted manner)?" and "Are additional external x-rays and intracervical radium advocated?" indicate need for further explanation.

We must reiterate that this work was done in order to explore the possibilities of intravaginal x-ray therapy alone. The technics of calculation necessitated certain set conditions in the placement of each cone in relationship with the geography of the upper vagina. We admit that in practice this accuracy cannot be obtained and there may well be overlapping of the fields and re-irradiation of folds of vaginal mucosa which are not displaced from the beam. However, in order to simplify each stylized treatment plan for purposes of comparison the doses assumed were designated by the amount to which the upper vagina was exposed in the whole treatment scheme. These doses were taken as air measurements. In clinical application it is necessary to individualize each treatment scheme and to regulate the actual exposures by observation of the reactions to each treatment.

As far as additional methods of irradiation are concerned no attempt was made in these calculations to add the effect of external x-rays or inter-

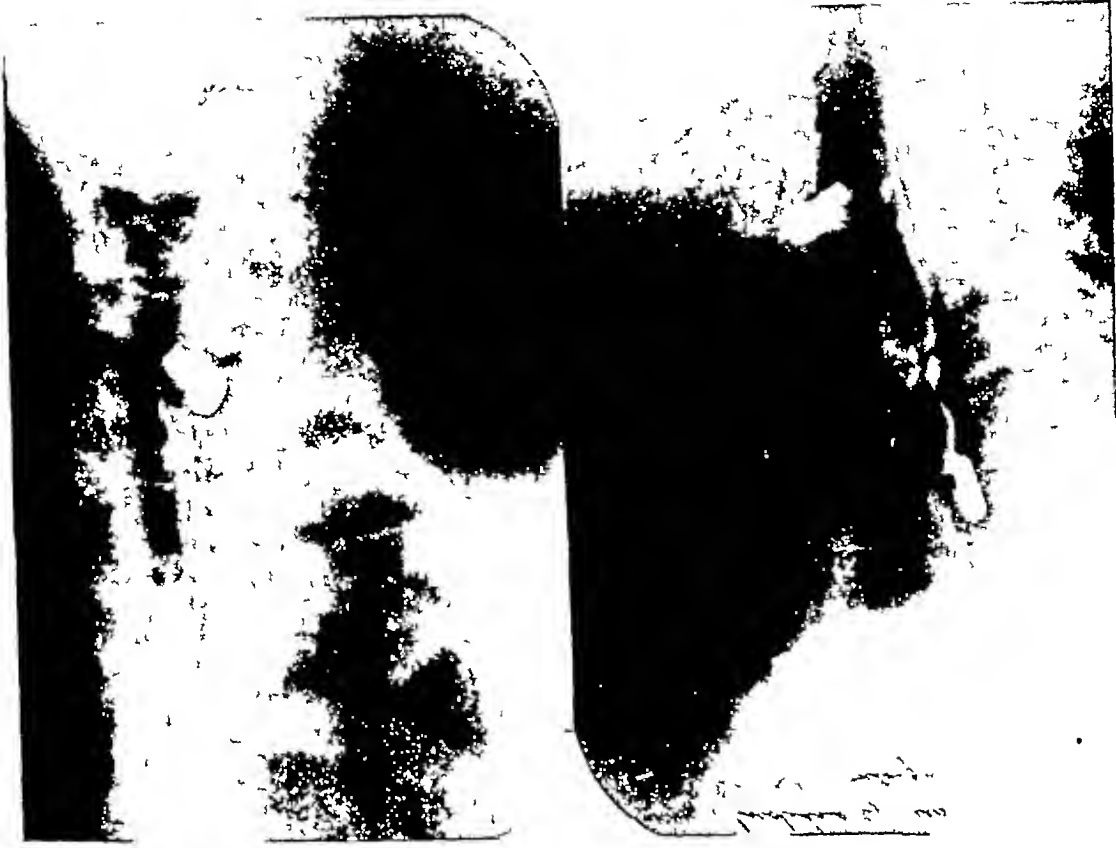


Fig 1 Small oesophageal-pharyngeal diverticulum

division of the recurrent laryngeal nerve. Herniation of the pharyngeal mucosa occurs between these muscles, which differ from each other in their innervation, physiologically, and morphologically.

In the early stage of the development of a pouch of this nature, symptoms are referable to derangement of the sphincteric operation of the cricopharyngeus, and the patient complains of mild dysphagia. This dysphagia may be present for a long time before a pouch is fully formed. In this early stage there is spasm of the strong sphincter guarding the oesophageal orifice, consequently, two divisions of the cricopharyngeus become separated, and the pharyngeal mucosa commences to herniate in the interval that is formed. Figure 1 illustrates a very early, and therefore small, diverticulum.

When the pouch is fully formed, symptoms are dysphagia, audible gurgling due to the displacement of air in the pouch,

excessive salivation, and regurgitation of unaltered particles of food. At a later stage a large pouch causes marked constriction of the upper end of the oesophagus by direct pressure. There is pronounced dysphagia for solids and liquids. The oesophageal orifice is much distorted. Figure 2 illustrates a large diverticulum.

The demonstration of these pouches is usually a very simple radiological procedure. In the last two years we have seen 22 of these in our practice, an incidence of 0.11 per cent. They are not a medical rarity.

DIVERTICULA OF THE THORACIC OESOPHAGUS

Diverticula of the oesophagus are usually seen immediately below the bifurcation of the trachea and in the lower two inches. To those situated below the bifurcation of the trachea Kragh (6) gave the name "tuberculous pouch." This term

Diverticula of the Foregut¹

DIGBY WHEELER, M A, M D, C M, M R C S (Eng), L R C P (Lon), F F R (Lon), F A C R

Winnipeg, Manitoba

EMBRYOLOGICALLY, the foregut is defined as being that part of the gastrointestinal tract which is proximal to the ampulla of Vater. In other words, the foregut includes the pharynx, the oesophagus, the stomach, and the duodenum. The distal inch of the oesophagus, the stomach, and the duodenum are supplied by the coeliac axis.

The workers of the Medical Faculty of the University of Manitoba have always shown an interest in diverticula. Grant (1), while Professor of Anatomy, published the first of his studies on duodenal diverticula, based on cadaver material. MacLean (2) was one of the early operators and was the first to remove a pouch imbedded in the head of the pancreas. The writer (3) has presented two papers dealing with the radiological aspects, the last report being in 1935.

Since 1935, as our experience has increased, we have observed a not inconsiderable number of diverticula of the foregut. The great majority of them have been incidental findings in routine barium examinations. Those at the oesophageal-pharyngeal junction and some of the oesophagus have been demonstrated as the result of an examination specifically directed to that part. The frequent demonstration of these lesions by our group is perhaps attributable to the fact that we are "diverticula conscious."

Despite the large number of papers, many of recent date, dealing with these diverticula, there still exists considerable confusion as to their classification, cause, and clinical importance. The descriptive term used by one author has apparently an entirely different meaning when used by a second. Odgers (4) divides all diverticula into primary and secondary and I

consider this to be the simplest and the best classification. The primary diverticula are those which occur without obvious cause. Their walls are formed by the mucosal and submucosal coats. Secondary diverticula are those having an obvious cause, with walls consisting of all coats of the bowel.

Synonymous terms used by various authors for primary diverticula are "false" and "congenital", for secondary diverticula, "true" and "acquired". The terms "pulsion" and "traction," as applied to diverticula, only confuse the issue, as it makes little if any difference clinically whether the sac has been pushed out or pulled out.

I shall consider diverticula in the following order: (i) oesophageal-pharyngeal diverticula, (ii) diverticula of the thoracic oesophagus, (iii) diverticula of the stomach, (iv) duodenal diverticula.

OE SOPHAGEAL-PHARYNGEAL DIVERTICULA

Raven (5) has presented an excellent study on oesophageal-pharyngeal diverticula and I am indebted to him for the anatomical details. These diverticula are usually situated posteriorly. They have been erroneously described as oesophageal. Actually the pouch is a prolapse of the pharyngeal mucous membrane between the two different sets of musculature comprising the cricopharyngeus. This muscle is composed of an upper superficial constrictor portion, which is part of the main pharyngeal constrictor musculature and derives its nerve supply from the pharyngeal plexus. The rest of the cricopharyngeus is composed of a lower, deeper sphincteric muscle, which blends posteriorly with the musculature of the oesophagus, forming a strong sphincter, and is innervated by several small branches from the inner

¹ From the Department of Radiology, University of Manitoba. Presented at the Second Inter-American Congress of Radiology, Havana, Cuba, Nov. 17-22, 1946.



Fig 3 Diverticulum of the thoracic oesophagus

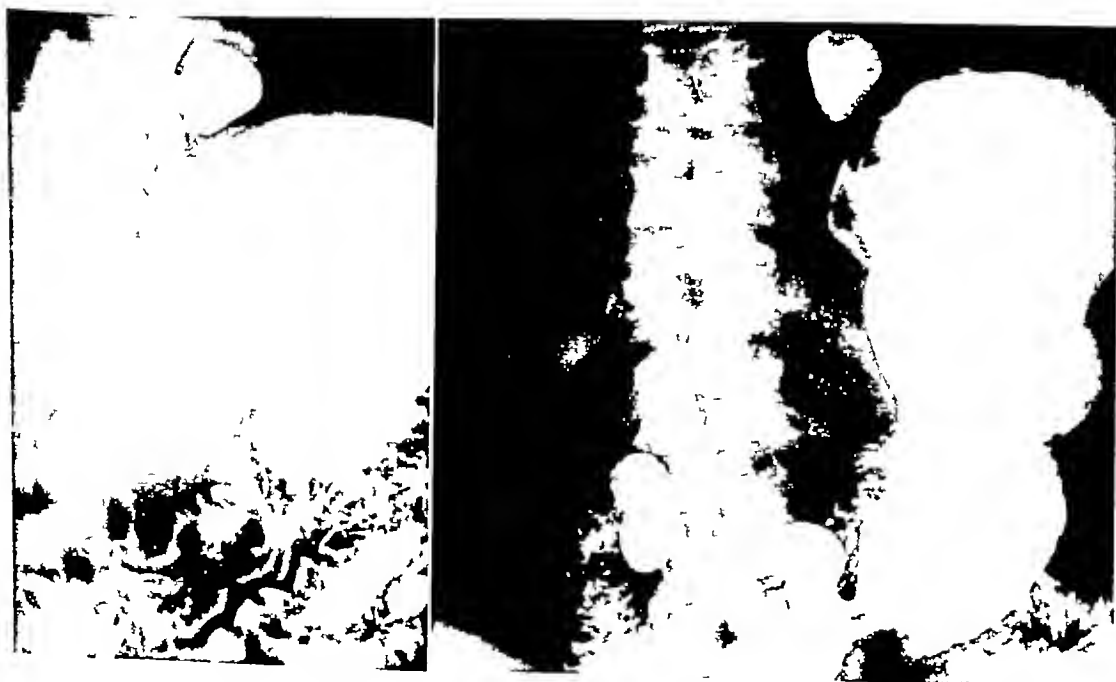


Fig 4 Diverticulum of the lower oesophagus



Fig 2 Large oesophageal pharyngeal diverticulum

is unfortunate. It is quite true that a number of these diverticula are seen in association with a tuberculous lymphadenitis, but many occur in patients in whom tuberculosis does not exist. The pouches are small and conical in shape with an oval orifice, and the long axis of the pouch runs obliquely upwards or downwards. The wall of the pouch often shows much irregularity. These diverticula may be single or multiple. We have seen 6 examples in the last two years. They have been found in the course of some 20,000 routine barium examinations, an incidence of 0.03 per cent. Figure 3 illustrates the radiological appearance.

In the same series, 3 cases of diverticula of the lower end of the oesophagus have been observed, an incidence of 0.015 per cent. It is said that a history of cardio-spasm can usually be elicited in these cases, but such a history was obtained in only one of our cases. The pouch is usually fusiform. Figure 4 illustrates a diverticulum in this position. In this par-

ticular case, though the lesion was an incidental finding and the patient had no symptoms referable to it, the hand of the surgeon could not be restrained.

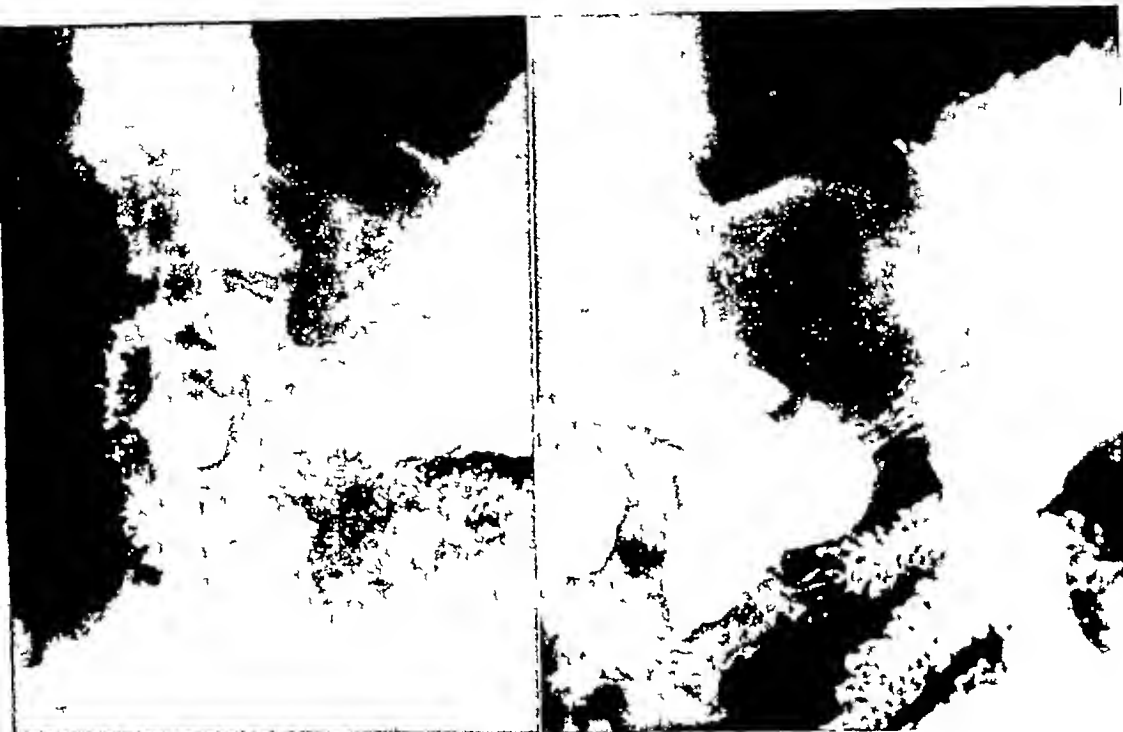
DIVERTICULA OF THE STOMACH

Our incidence of diverticulum of the stomach is 0.1 per cent, a somewhat lower figure than that recorded by other authors as reported by Frank (7). These diverticula have all been found at the cardiac end of the stomach on the lesser curvature.

The symptomatology is quite inconclusive. Indeed, it is doubtful if any complaints at all can be explained on the basis of these diverticula. It is emphasized that they are an incidental finding in the radiological examination. Figure 5 demonstrates a diverticulum of the stomach.

DIVERTICULA OF THE DUODENUM

Grant, in his study of cadaver material, showed a percentage incidence of 11.3 for duodenal diverticula. This is higher than



Figs 6 and 7 Two examples of duodenal diverticula

any symptoms can be attributed to them. No complete case of obstruction of the ducts of the pancreas or liver is on record, and only in some cases has a partial obstruction been noted. It would appear that the important considerations are the imbedding of the diverticulum in the pancreas and the presence or absence of free drainage. When these diverticula give trouble, it is usually because of inflammation of the wall, which is of extremely rare occurrence.

CONCLUSIONS

- 1 Diverticula of the different portions of the foregut have been described and illustrated.
- 2 The incidence of the various diverticula is given.
- 3 With the exception of the diverticula at the pharyngeal-oesophageal junction, they are usually incidental findings.
- 4 The oesophageal-pharyngeal diverticula produce definite symptoms. The others are practically asymptomatic.
- 5 Diverticula of the lower oesophagus

are important when instrumentation is contemplated.

6 Because diverticula are so readily demonstrated by x-ray, their significance, except for the oesophageal-pharyngeal type, has been greatly exaggerated.

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- 5 RAVEN R W Diverticula of Pharynx and Oesophagus *Lancet* 1 1011-1015 May 13, 1933
- 6 KRAGH J *Acta oto laryng* 4 49 1922
- 7 FRANK L L Diverticulum of Stomach *Am J Roentgenol* 52 511-513 November 1944
- 8 CASE J T Diverticula of Small Intestine, Other Than Meckel's Diverticulum *J A M A* 75 1463-1469 Nov 27 1920
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- 10 SPRIGGS E I AND MARVER O A Intestinal Diverticula *Brit M J* 1 130-134, Jan 23, 1926, *Quart J Med* 19 1-34, October 1925



Fig 5 Diverticulum of the stomach

the percentage 1.42, quoted by Baldwin, and 3.3, quoted by Linsmayer. In considering the frequency of diverticula as demonstrated by x-ray examination, we encounter a wide variation in percentages. One would not expect so high a percentage as is found in cadaver material for two reasons. First, the age incidence of the cadaver group would certainly be higher than the age incidence of the patients presenting themselves for routine gastro-intestinal examinations. Secondly, it is obvious that to fill a duodenum with paraffin and then to open the duodenum and search for pouches is a more accurate and certain method than visualization with the aid of an opaque medium. Case (8), in a series of 6,847 consecutive barium meal studies, demonstrated duodenal diverticula in 1.2 per cent of cases, Andrews' (9) percentage was 0.18, and that of Spriggs and Marver (10) 3.8. Our incidence as determined by reviewing the reports on the last 20,000 barium series is 5.1 per cent. This is somewhat lower than the incidence previously reported when a smaller series was reviewed. It is pointed out that in the compilation of these statistics only diverticula of the primary type were considered, that is to say, those arising from the second, third, and fourth portions of the duodenum. No

case of secondary diverticulum, pouching of the duodenal cap, the result of stenosis due to an ulcer, has been included.

Included in our group of primary diverticula of the duodenal loop are diverticula of all sizes, some very small, no larger than a pea, and some very large. A number of the diverticula arise adjacent to the ampulla of Vater. Care has been taken not to include dilatation of the ampulla as a diverticulum. It is again pointed out that secondary diverticula have not been included in the study.

Primary diverticula of the duodenum have the following characteristics:

- 1 They are found only in the second, third, and fourth portions of the duodenum.
- 2 They are found on the inside of the duodenal loop and are therefore in relationship to the head of the pancreas.
- 3 They are often multiple. They are often seen as goblet-shaped protrusions of the mucous membrane, communicating with the lumen of the duodenum by a narrow neck.
- 4 They vary in size from that of a small pea to that of a walnut.
- 5 They are more frequently seen after the fifth decade.

Figures 6 and 7 demonstrate diverticula of the duodenum.

One would expect considerable pathological disturbance to be associated with duodenal diverticula, both because of their frequently large size and because they are situated on the inside of the duodenal loop. Here they may produce stenosis of the duodenum, affect the bile ducts, or irritate the pancreas. The absence of inflammatory processes is probably due to (a) sterility of the duodenal contents, (b) the retroperitoneal position which allows for their distention, (c) free drainage back into the bowel.

Despite the frequency of these diverticula and the fact that they are often very large, it is surprising how infrequently



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Medical, Biological and Industrial Applications of Monochromatic Radiography and Microradiography¹

GEORGE L. CLARK, Ph D, D Sc

Department of Chemistry, University of Illinois

CERTAINLY THERE IS nothing new in the idea of using an x-ray beam of essentially a single wave length (monochromatic) in contrast with the usual beam of many wave lengths (polychromatic) in the various branches of radiography, including roentgen diagnosis. In the high state of development of this science in the hands of roentgenologists to the point of delineation of extraordinarily fine detail, the question is naturally asked, what is to be gained? It seems of interest to give an account of a renewed experience of several years, particularly during the war, with monochromatic radiography. For this subject crops up anew as the result of a newly developed microradiography, in which radiographs of small objects are photographically enlarged up to 300 or 400 diameters. Therein lies the critical test of monochromatic vs polychromatic technic.

A brief review of the principles of x-ray spectroscopy will suffice as a basis for consideration of monochromatic radiography.

1. At all voltages and with x-ray tube targets of all chemical elements, a general or continuous spectrum characterizes the radiation generated. It is only above a certain critical voltage that the characteristic line spectrum of the target element is generated. Thus, at all voltages below 69,300, the tungsten target tube generates in the range of shortest wave lengths only the continuous or polychromatic beam with a short wave-length limit, λ_0 , determined by the voltage in accordance with the Duane-Hunt application of the Planck-Einstein equation or $Ve = hc/\lambda_0$, where V is the voltage, e the electronic charge, h the Planck quantum constant, and c the velocity of light. Above 69,300 volts

there appear the K-lines of the characteristic tungsten spectrum superposed on the continuous spectrum, with the result, of course, that certain wave lengths, particularly the $K\alpha_1$ line at 0.2086 Å U are greatly intensified. The much softer rays of the L, M, N series are generated at correspondingly lower voltages.

To isolate this characteristic $K\alpha_1$ ray would be to produce a monochromatic beam. There is only one way of accomplishing this strictly, and that is selection and reflection by a crystal, but the very great loss in energy renders the method impracticable. The more common practice is use of a characteristic filter, for which the K absorption edge lies between $K\beta$ and $K\alpha$, cutting out the shorter rays, including $K\gamma$ and $K\beta$, but transmitting the $K\alpha$ doublet and all longer rays. This process is also impracticable for tungsten rays, because of the high intensity of the general radiation at 70,000 volts and above, and because of the fact that some exceedingly rare element such as lutecium or ytterbium is required for the filter. Thus the attempt to isolate a single wave length from the tungsten rays is confronted with almost insurmountable obstacles, not only from a practical standpoint, but even for purely academic experimentation. For considerable penetration and for relatively thick sections in the practice of radiography, it is still essential to use the highly complex polychromatic beam from the usual tungsten target.

X-ray diffraction analysts have long been familiar with and made use of tubes which do, however, produce essentially monochromatic beams. For example, a molybdenum target will generate the very intense characteristic K-rays at 20,000

¹ Presented at the Thirty second Annual Meeting of the Radiological Society of North America, Chicago Ill., Dec 1-6, 1940.

SUMARIO

Divertículos del Prozogaster

Bajo el título anterior considéranse divertículos esófago-faríngeos y divertículos de la porción torácica del esófago, del estómago y el duodeno. En una serie de 20,000 exámenes corrientes con bario, ejecutados durante los dos últimos años, la incidencia de los varios divertículos fué: divertículos esófago-faríngeos, 0.11 por ciento, divertículos de la porción torácica del esófago, precisamente más abajo de la bifurcación de la tráquea, 0.03 por ciento, y en el extremo inferior del esófago, 0.015 por

ciento, divertículos gástricos, 0.1 por ciento, divertículos duodenales, 5.1 por ciento.

Por virtud de la facilidad con que se descubren roentgenográficamente, se ha exagerado sobremanera la importancia de los divertículos del prozogáster. La forma esófago-faríngea puede ocasionar disfagia, sialorrea y regurgitación alimenticia. Los demás suelen ser asintomáticos, encontrándose sólo fortuitamente al efectuar exámenes corrientes.



In order to compare the contrast obtainable with the two types of x-ray tubes, radiographs were made of an aluminum step wedge. This wedge was constructed of strips of aluminum 0.010 in thick. Ten of these strips of successively shorter length were combined to give a wedge consisting of ten steps covering the thickness range of 0.010–0.100 in of aluminum.

density of the first step on the radiographic image the same in all cases. The two radiographs on each type of film were developed simultaneously. The film was placed in contact with the step wedge in every case. Experimental conditions are given in Table III. Typical step radiographs have been published by Clark and Eyler (1).

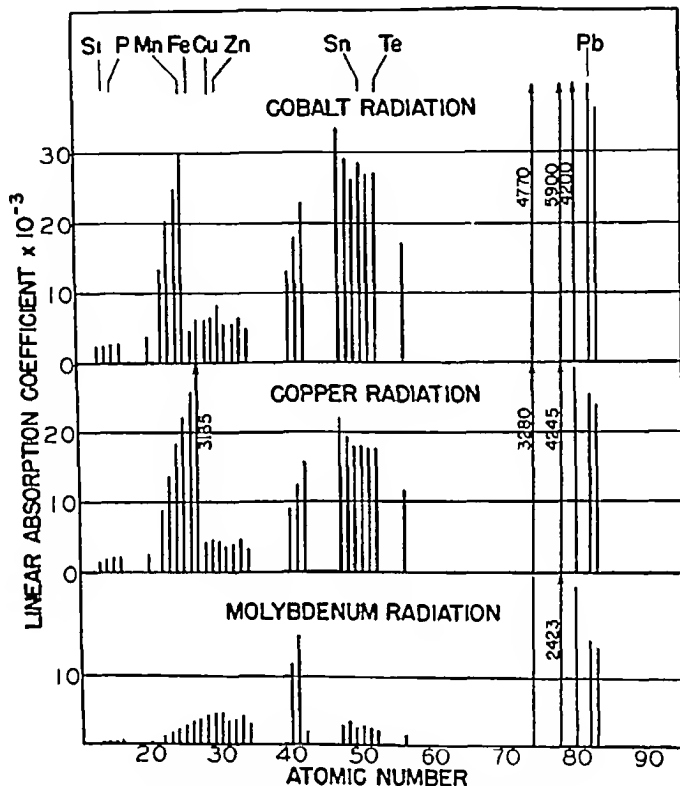


Fig 1 Linear absorption coefficients for molybdenum, copper and cobalt monochromatic radiation

The wedge was masked with lead to eliminate scattered radiation, and a lead foil 0.010 in thick was placed behind the film.

Radiographs using both types of radiation were made with Agfa Non-screen film and Eastman Type A film. The latter has a fine-grained emulsion and is designed for use in radiography when higher contrast is desired. Agfa Non-screen is a film with a coarser-grain emulsion and its use makes possible a reduction in exposure time. Milliamperage and exposure time were governed to make the

TABLE III

Pattern Number	Target Element	Kilo-voltage	Milli-ampere-Seconds	Focal Spot-Film Distance (in)
1	W	40	11	30
2	W	40	51	30
3	Mo	40	2	30
4	Mo	40	9	30

Densities of the images of the steps on the radiographs were measured with a Leeds and Northrup recording microphotometer. These densities are plotted against the number of the step corresponding to a given

volts, where the general radiation is still very weak. When filtered through a very thin layer of a zirconium compound with no serious loss in intensity, the tremendously predominating $K\alpha$ doublet characterizes the beam as essentially "dichromatic," with a wave length of 0.71 Å. Similarly other commonly available diffraction tubes have the following targets listed in comparison with those just discussed (see Table I).

TABLE I

Target	K Series Excitation Voltage	Predominating Wave Length ($K\alpha_1$ Doublet)	Filter
Tungsten	69,300	0.21 Å	?
Molybdenum	20,000	0.71 Å	Zirconium
Copper	8,860	1.54	Nickel
Cobalt	7,710	1.79	Iron
Iron	7,100	1.93	Manganese
Chromium	5,980	2.286	Vanadium

It is clear, therefore, that such tubes operated below 50,000 volts produce beams so nearly of known predominating wave lengths that the whole science of diffraction analysis from sharp line patterns has been made possible, and the lower the voltage the farther from general radiation and the nearer the approach to a monochromatic beam such as would be isolated perfectly only with the crystal spectrometer. Therefore, the application to radiography is necessarily limited to thin sections.

2. What, then, is the theoretical advantage of monochromatic radiation?

Radiographic detection of inhomogeneities in an object depends upon a difference in absorption of λ -radiation by different portions of the object. The most heavily absorbing regions of the object placed between the x-ray tube and the photographic film decrease the intensity of radiation reaching the film and lead to a lower photographic density of the film under that region.

The absorption of λ -radiation follows the equation

$$I = I_0 e^{-\mu x}$$

where I is the intensity of radiation of initial intensity I_0 , after passage through

x centimeters of homogeneous material, e is the base of natural logarithms, and μ is the linear absorption coefficient. Differences in absorption of x-rays in various parts of an object may arise either from different values of the absorption coefficient or from variations in thickness of material in the different parts.

Values of the mass absorption coefficient μ/ρ (where ρ is the density) for different elements as a function of the wave length of the λ -rays absorbed have been determined. The mass absorption coefficient is a function of atomic number and for a given element increases with an increase in wave length of the λ -rays absorbed. The data listed in Table II for aluminum as absorber will illustrate this variation.

TABLE II

Wave Length of X-radiation Å	Mass Absorption Coefficient for Aluminum
0.5604	2.74
0.6149	3.60
0.7097	5.30
1.5392	48.7
1.6565	58.4
1.9344	92.8
2.2869	149

The laws of absorption apply to single wave lengths as demonstrated in Figure 1 for the $K\alpha$ rays of molybdenum, copper, and cobalt, commonly used as targets. It is self-evident that there must be the sharpest delineation of radiographic detail with a monochromatic beam properly selected. Three photographic properties must be considered in a radiographic method, namely, contrast or sensitivity, latitude, and definition. Assuming not too wide a range of thicknesses, contrast and definition are of greatest importance.

It now becomes significant to compare the performance of a tungsten and a molybdenum target tube, both operated at 40,000 volts and with identical radiographic techniques as to size of focal spot, distance from focal spot to specimen and of specimen to film, identical film, and simultaneous development.

In order to compare the contrast obtainable with the two types of x-ray tubes, radiographs were made of an aluminum step wedge. This wedge was constructed of strips of aluminum 0.010 in thick. Ten of these strips of successively shorter length were combined to give a wedge consisting of ten steps covering the thickness range of 0.010–0.100 in. of aluminum.

density of the first step on the radiographic image the same in all cases. The two radiographs on each type of film were developed simultaneously. The film was placed in contact with the step wedge in every case. Experimental conditions are given in Table III. Typical step radiographs have been published by Clark and Eyer (1).

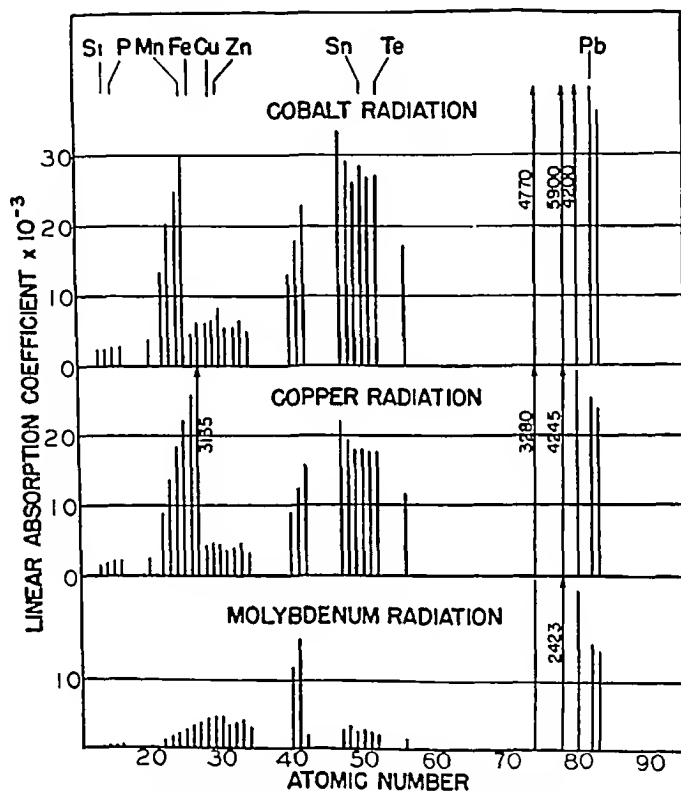


Fig 1 Linear absorption coefficients for molybdenum, copper, and cobalt monochromatic radiation

The wedge was masked with lead to eliminate scattered radiation, and a lead foil 0.010 in thick was placed behind the film.

Radiographs using both types of radiation were made with Agfa Non-screen film and Eastman Type A film. The latter has a fine-grained emulsion and is designed for use in radiography when higher contrast is desired. Agfa Non-screen is a film with a coarser-grain emulsion and its use makes possible a reduction in exposure time. Milliamperage and exposure time were governed to make the

TABLE III

Pattern Number	Target Element	Kilo-voltage	Milli-ampere-Seconds	Focal Spot-Film Distance (in.)
1	W	40	11	30
2	W	40	51	30
3	Mo	40	2	30
4	Mo	40	9	30

Densities of the images of the steps on the radiographs were measured with a Leeds and Northrup recording microphotometer. These densities are plotted against the number of the step corresponding to a given



Fig 2 Radiograph of aluminum alloy casting made with monochromatic molybdenum rays showing hair-line cracks (cold shuts)

density The step number is 100 times the thickness of the step in inches It is easily apparent that there is a markedly greater change in density per step for the molybdenum characteristic ray than for the tungsten polychromatic beam

Definition may be illustrated with a wartime experience The following work on development of a radiographic technic was undertaken at the request of the authorities at Wright Field, Dayton, Ohio

In the production of an aluminum alloy aircraft motor casting, the casting process leads to frequent occurrence of so-called "cold shuts," caused by failure of two advancing fronts of molten metal to fuse upon meeting These defects occur near the upper front flange and above the ports of the casting The metal of the top deck of the casting, in which the flaws occur, is approximately 5/16 in in thickness and the shuts, which have the appearance of very fine regular cracks, may extend completely or only partially through the metal Very shallow shuts are important, since they might lead to a crack extending through the entire section under the influence of vibration Since the area involved encloses the cooling system, loss of cooling fluid and subsequent failure of the motor may follow The defects are a few thousandths of an inch wide and may be up to an inch in length

The previous method of inspecting these castings involved a leakage test and breaking-up of castings In the leakage test,

the casting is immersed in water and compressed air is forced into the cooling system This test will detect any defects extending completely through the wall Shallow defects, however, which might open under the influence of vibrational stress are not detected The breaking test involves selecting a number of castings at random A specified fraction of these are sawed and broken apart and the suspected regions are inspected visually This test, however, is wasteful and leaves much to be desired in the certainty of the results The attempt to develop a radiographic method arises from the desire to use a more certain method which is non-destructive, and one which will detect more shallow defects than are found by the leakage test

The fact that the castings are constructed of a metal of low density and the fact that shallow defects may assume considerable importance suggested the necessity of using a low tube voltage in order to obtain the highest possible contrast The ordinary commercial radiographic x-ray tube with tungsten target is oil-immersed for cooling, thus making possible continuous operation In addition, the port for emission of the x-rays is made of glass These two features lead to considerable inherent filtration in the x-ray tube itself, involving a filtering out of the longer wave lengths useful in obtaining higher contrast Consequently, the possibility of using a diffraction type of tube with beryllium windows and water-cooled target was investigated

Two possible advantages in the use of a molybdenum diffraction tube presented themselves In the first place, the inherent filtration in the tube should be considerably less than in the case of an oil-immersed tube In the second place, convenient tube voltages of 30 to 40 kv could be used without sacrifice of contrast because of the greater intensity of characteristic radiation as compared with the general radiation, and because the wave length of the characteristic radiation does not change with increase in voltage In effect, then, this technic involves pro-

duction of radiographs with very nearly monochromatic radiation, radiographically speaking, with a wave length of 0.71 Å.U. The use of a tube with a tungsten target and operated at 30 to 40 kv is hindered by the inherent filtration of the tube, previously discussed.

Without discussing the details of arrangement, it may be asserted that the use of monochromatic molybdenum radiation alone made the inspection possible, for tungsten polychromatic radiation did not provide sufficient contrast or definition to detect any of the cold shuts in 24 castings investigated. These fine hair-like

50 kv, 5 ma, 10 ft distance, delivered 11.5 r in 20 minutes, or 4.4 r in 7 minutes, 42 seconds, which was cut down to 3.5 r when a zirconium filter was used to isolate the $K\alpha$ doublet at 0.71 Å.U. This 2.6-fold greater dosage in a given time at this relatively great distance was most surprising, but has been borne out repeatedly in all experiments.

Next, a series of highly quantitative experiments have been run under many conditions to calibrate intensifying screens of two types when used with the two types of radiation. It is interesting to note that, in spite of this comparatively soft

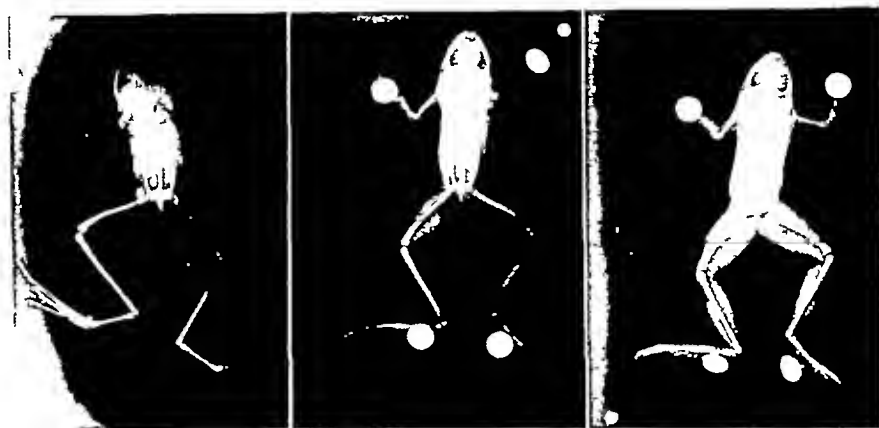


Fig 3 Radiographs of small frog made with monochromatic radiation and polychromatic radiation. From left to right: chromium monochromatic, molybdenum monochromatic, tungsten general radiation. All at 36 kv.

cracks are easily seen in the molybdenum radiograph reproduced in Figure 2.

Speed is also an important consideration in radiography, especially where motion is involved. New quantitative measurements comparing a Machlett molybdenum tube with beryllium-foil windows and a standard oil-immersed tungsten radiographic tube follow. The former was operated in a Hayes diffraction unit capable of operating up to 50 kv, the latter in a Picker 150 kv mobile radiographic unit. The final tests were made at a distance of 10 ft, the tungsten target tube at 50 kv and 5 ma delivered 4.4 r in 20 minutes, the maximum in the general radiation curve at this voltage is at 0.46 Å.U. The molybdenum target tube at

radiation, the films have been enclosed in regular aluminum cassettes and intensifying screens used both front and rear with remarkable success. From a mass of data used to calibrate exposures and screen speeds a few may be selected here for comparative purposes (distance 10 feet), as shown in Table IV.

This table demonstrates not only the relative speeds, but also the necessity of calibration of radiation with screen types at different excitation potentials, a matter which evidently is frequently neglected in diagnostic procedures. Under the same conditions of distance, voltage, and exposure, the monochromatic molybdenum rays are of the order of 2 1/2 times as fast with fluorazure screens as the tungsten

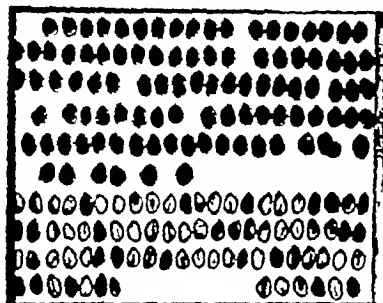
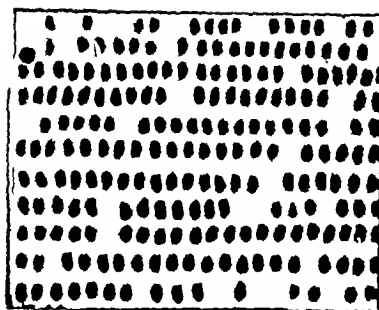


Fig 4 Radiographs of pine seeds with polychromatic general radiation, tungsten (above) and monochromatic molybdenum radiation (below)

general radiation for the particular tubes used. It must be remembered that the molybdenum-target tube has beryllium-foil windows as commercially produced, while the tungsten-target tube is of the standard 150-kv diagnostic type. However, a few experiments have been run with a tungsten target tube fitted with beryllium windows, of the type described by T. H. Rogers (2). Under conditions of these comparisons there is relatively little effect of the windows.

Although speed factors are decidedly favorable from the molybdenum tube, another advantage would outweigh these, even if they were distinctly unfavorable, namely, definition.

A typical industrial application requiring the extreme in radiographic definition, namely, the detection of cold shuts in aluminum alloy airplane motor castings, has already been cited. It seemed appropriate to illustrate some of the problems of biology and medical diagnosis with molybdenum monochromatic vs tungsten poly-

chromatic radiation. Examples were a small frog, a hand, and a skull. Radiographic technique may be illustrated for the skull. Assuming a common procedure of 68 kv, 12.5 ma-seconds, 36 in distance, and parspeed screens, and accepting a principle of doubling exposure in ma-seconds for a drop of 14 kv, the molybdenum monochromatic radiation is generated at 48 kv for 50 ma-seconds with

TABLE IV

Target	Screen	Voltage (kv)	Milliampere seconds	Light Meter Reading Relative Transmission
Tungsten	Parspeed	40	10	58
	Fluorazure	40	10	25
	Parspeed	50	10	27
	Fluorazure	50	10	9.5
Molybdenum	Parspeed	40	10	43
	Fluorazure	40	4	36
	Parspeed	50	10	20
	Fluorazure	50	4	16
Tungsten	Parspeed	70	10	10
	Fluorazure	70	10	3
	Parspeed	80	10	5
	Fluorazure	80	10	2
	Parspeed	90	10	3.5
	Fluorazure	90	10	2

parscreens, and 20 ma-seconds with fluorazure screens, and with tungsten radiation and fluorazure screens for 50 ma-seconds. At this low potential there is not so good penetration through the skull proper as at higher values, but the detail in the softer structures, sinuses, pituitary, etc., is all that could be desired. Sharpness of detail is best indicated by enlargement of particular areas, or projection on a screen. The advantage is all with the molybdenum radiation. Trabeculation and canaliculi are clearly disclosed without enlargement with this monochromatic beam, but these extremely fine details of structure are not resolved in the tungsten radiographs. Figure 3 shows a comparison of radiographs at 36 kv, of a small frog, made with monochromatic chromium (2.286 Å U), monochromatic molybdenum (0.71 Å U), and general radiation from a tungsten target.

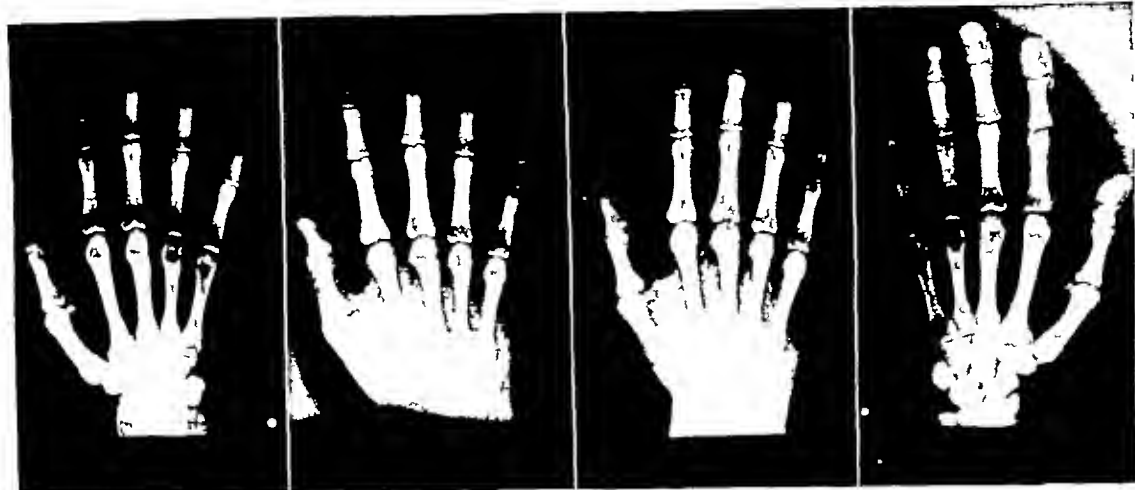


Fig 5 Radiographs of hand made with monochromatic radiation, arranged in order of increasing wave length, left to right molybdenum, copper, cobalt chromium

These examples, achieved by amateurs in diagnostic radiography, are meant merely to suggest possibilities, for the most incipient pathological conditions might well be detected under the extraordinary resolution of beams of essentially one wave length. Molybdenum target tubes are commercially available, and easily operated up to 50,000 volts and 20 ma continuously. Manufacturers might easily modify the construction to reach 70,000 volts safely, with consequent increase in intensity of $K\alpha$ rays, but also generation of more intense and harder general radiations, which must be filtered out with zirconium. Figure 4 illustrates the far greater sharpness of details of pine seeds radiographed with monochromatic molybdenum rays than that obtained with tungsten general radiation (standard diagnostic tube) at the same voltage.

By way of comparison, filtered monochromatic rays (actually "dichromatic" or the $K\alpha$ doublet) of molybdenum, copper, cobalt, and chromium, derived from diffraction tubes at 40,000 volts, have been used for radiographs of the hand (Fig 5). As the wave length becomes longer in the order of targets as given, the soft tissues, tendons, nails, etc., appear more and more clearly in sharp detail. Is there not a place, particularly in the larger research institutions, for a multiple selective mono-

chromatic radiography? With proper choice of wave length adapted to a particular tissue or problem, perhaps two, three, four, or five exposures may be made, each bringing out its own constituents, or details of fine structure. For this is the technique which has made microradiography possible, the parent science of radiography (1:1 in the sense of relation of size of specimen to image) may easily profit by this experience.

MICRORADIOGRAPHY

Attempts to produce enlarged radiographs of small heterogeneous specimens date back to 1913, and the names of Goby, Dauvillier, and Lamarque appear in several publications on biological materials especially. It was recognized that an enlarged radiographic image could be obtained in two ways (1) increasing the distance from specimen to plate and (2) photographic enlargement of an image registered on fine grain emulsion. By consideration of absorption indices these authors also limited their efforts to very low voltage of the order of 4,000 to 8,000, at which potentials, of course, only soft general radiation was generated. These efforts were not generally successful as medical and biological techniques. Increasing distance from specimen to plate to gain enlargement only served to de-

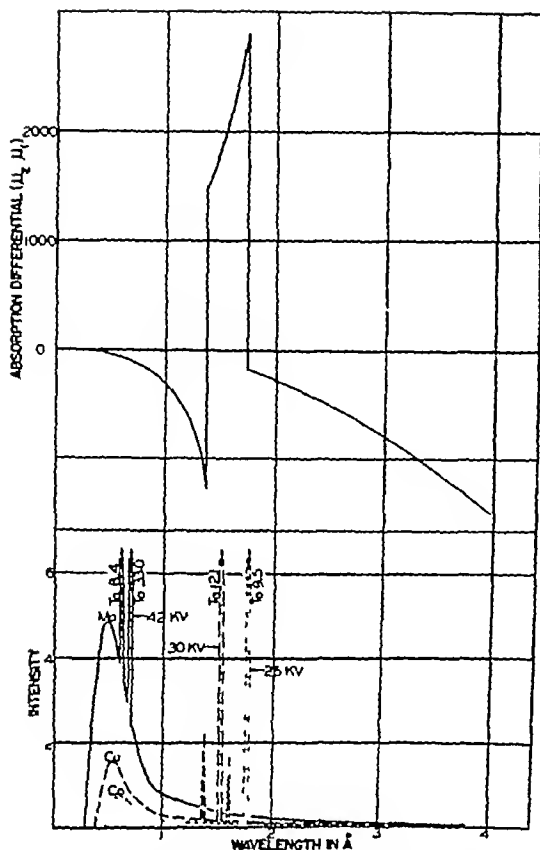


Fig 6 Diagram illustrating choice of monochromatic radiation in microradiography for maximum differentiation (after Maddigan)

crease sharpness and definition, even though smaller and smaller focal spots were tried. Suitable tubes for such soft radiation were not generally available, and at best photographs had to be made in vacuum. Nor were suitable fine-grained photographic emulsions available to enable magnifications to a useful range of 100 diameters or above. Some improvements were made in France and Russia, but in 1938 microradiography was still in a largely unsatisfactory and unused state. In that year the author obtained in Belgium some Gevaert Lippmann emulsion, in which the silver halide grains are of the order of $1/10,000$ as large as in ordinary roentgen film. With this, experiments were made with monochromatic radiation from molybdenum, copper, cobalt, iron, and chromium targets, generated at 20,000 to 30,000 volts in com-

mercially available diffraction equipment, thus eliminating necessity for vacuum technics. Granting that the differential between linear absorption coefficients for two constituents is less favorable even for the chromium $K\alpha$ radiation than for a single ray generated at 4,000 volts, yet the advantages in ease, speed, contrast detail, and sharpness of the monochromatic ray *far outweighed* the greater differential absorption of the *polychromatic* beam at 4,000 volts. The result has been a successful development beyond all expectations.

The first successful application was to complex alloy systems in which detection of phases as well as submicroscopic cracks, flaws, porosity, etc., presented a major problem. In this connection arose the use of multiple radiations for bringing out, one step at a time, complex structures of five or more components. Taking the simple case of two components (Fig 6) the $\mu_1 - \mu_2$ values are plotted as a function of wave length from known tabulated data (for example, a copper-aluminum alloy). At some wave length will appear a peak representing maximum difference between μ_1 for copper and μ_2 for aluminum, at another wave length the curve may cross a zero axis and at still another a large negative value when $\mu_2 > \mu_1$. Obviously a monochromatic ray can be chosen, usually the $K\alpha$ ray, which will fit into these peaks and thus produce the maximum differentiation in blackening, and in detail on the plate. For a second pair of components another wave length is the optimum selection. One phase may appear black with one radiation and white with another, along with all gradations of grays. This multiple selective technic solved problems of great complexity and of utmost wartime importance. Figure 7 illustrates typical microradiography of a copper-beryllium alloy which had extensive use during the war. Figure 8 shows incipient crystallization of two salts.

With biological tissues there are usually involved varying densities or thicknesses of very similar materials composed of

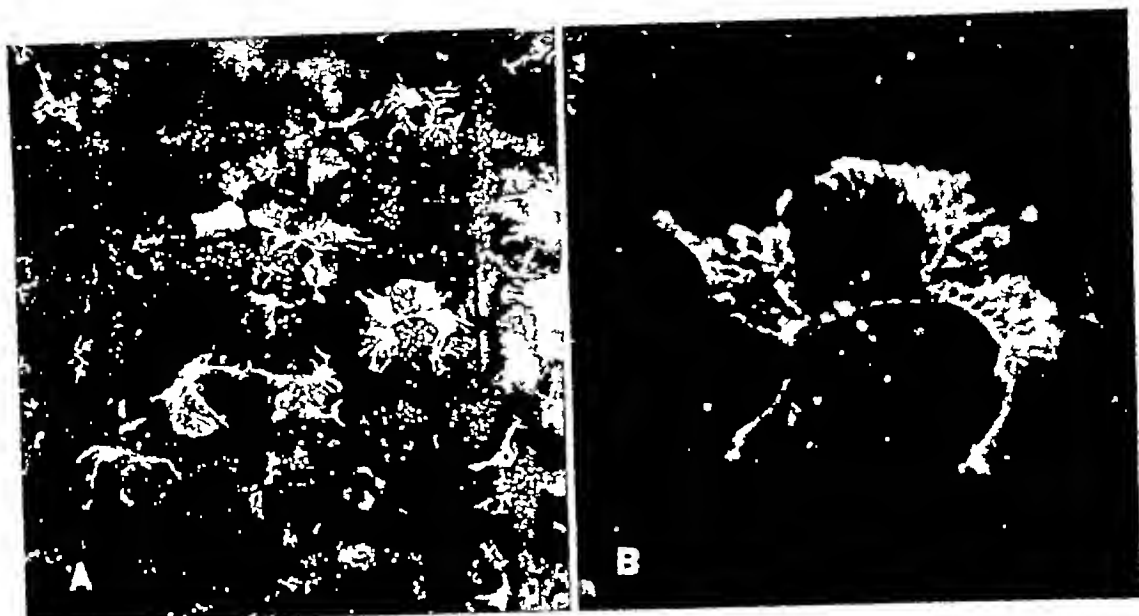


Fig 7 Microradiography of copper beryllium alloy showing phase structure A $\times c 75$ B Enclosed area from A, $\times c 300$

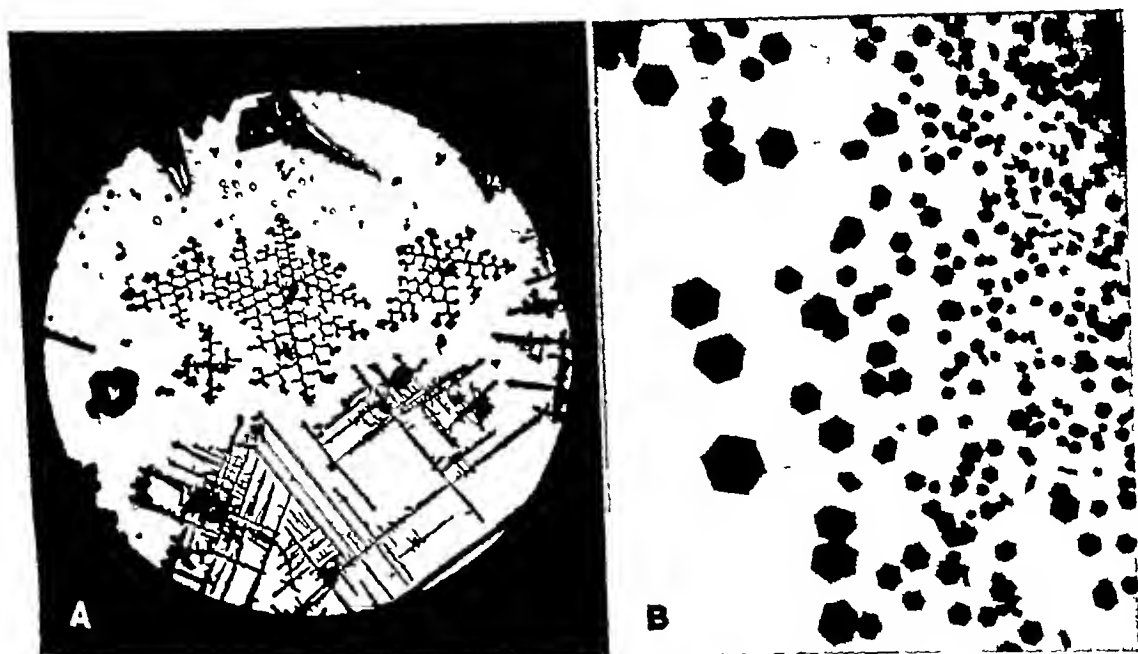


Fig 8 Typical microradiographs of incipient crystallization A Silver chromate B Cesium bismuth iodide $\times c 100$

carbon, hydrogen, oxygen, nitrogen, etc, rather than phases of markedly differing absorbing power. But here again the far greater sensitivity of the monochromatic ray in contrast and definition make it possible to delineate the finer structure of

tissues. Then there is always available the "staining" technique with differentially absorbing materials such as thorocontrast, lead and mercury salts, iodized oils, gases, and other agents already familiar in macro-radiography. Illustrated in Figures 9, 10,

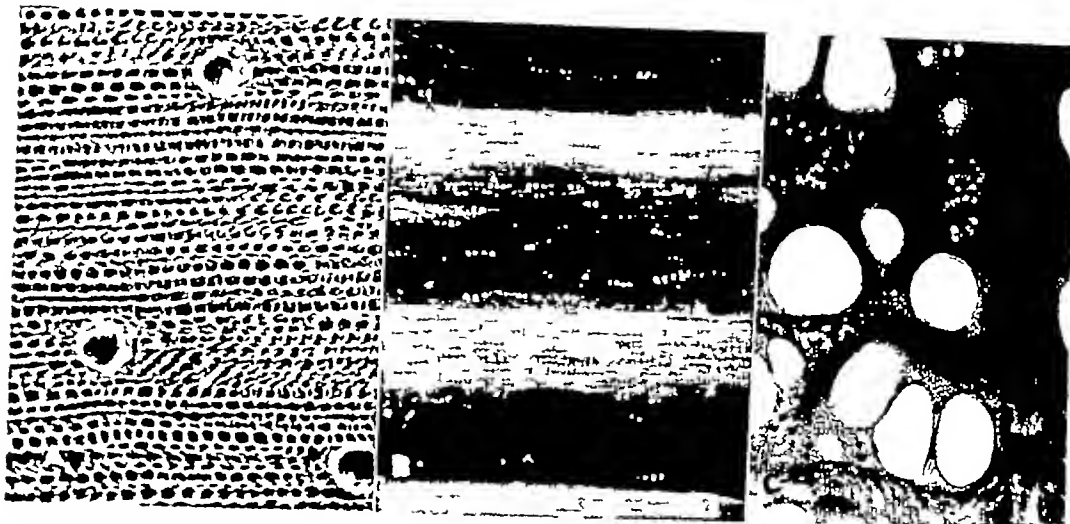


Fig 9 Microradiographs with monochromatic radiation of oakwood sections A Tangential B Radial C Transverse $\times 600$

and 11 are several examples of biological materials with and without impregnation

The technic is remarkably simple. A sample sliced with a microtome is placed in close contact with the Lippmann film or the 548-0 Eastman emulsion, which is satisfactory and much faster. Thickness depends on resolution desired in this three-dimensional registration, varying from a few microns up to 100 microns or more. Exposures to the monochromatic beam are of the order of one to six minutes. A small cassette covered with black paper or opaque plastic may be used, or a small camera attached directly to the head of the diffraction tube without an intervening layer of light-protective material, inasmuch as the filter for rendering the beam monochromatic shuts out light, as does the beryllium-foil window of the tube itself. The image is developed and then enlarged with the microscope up as high as $400\times$.

Medical and biological microradiography by simple routine procedures is still new. In the hands of histologists and diagnosticians its possibilities are limitless, supplementing and augmenting the microscope. Its practical success has arisen from use of monochromatic beams, generated by commonly available equipment. The microradiograph at $400\times$ has caused this re-

examination of classical macroradiography at $1\times$. Is it rash to predict that the molybdenum target tube, and indeed copper, cobalt, iron, chromium and others, may take its place along with the usual tungsten target diagnostic tube in progressive and research-minded radiological laboratories? And certainly there is yet much to be done in therapy and investigation of biological and chemical effects with these selected beams of essentially a single wave length.

SUMMARY

1 The use of essentially monochromatic roentgen rays, especially the $K\alpha$ doublet from a molybdenum target with a wave length of 0.71 \AA is demonstrated for diagnostic radiography in certain cases in comparison with tungsten radiation generated at the same voltage and current.

2 Dosage from commercially available diffraction tubes with molybdenum target is markedly greater at 10 feet than that from the usual diagnostic tubes.

3 The necessity of calibrating the speed of intensifying screens is experimentally shown.

4 Appreciably greater definition in fine detail is produced in monochromatic radiographs. Examples illustrated are extremely fine hair-line cracks in castings,

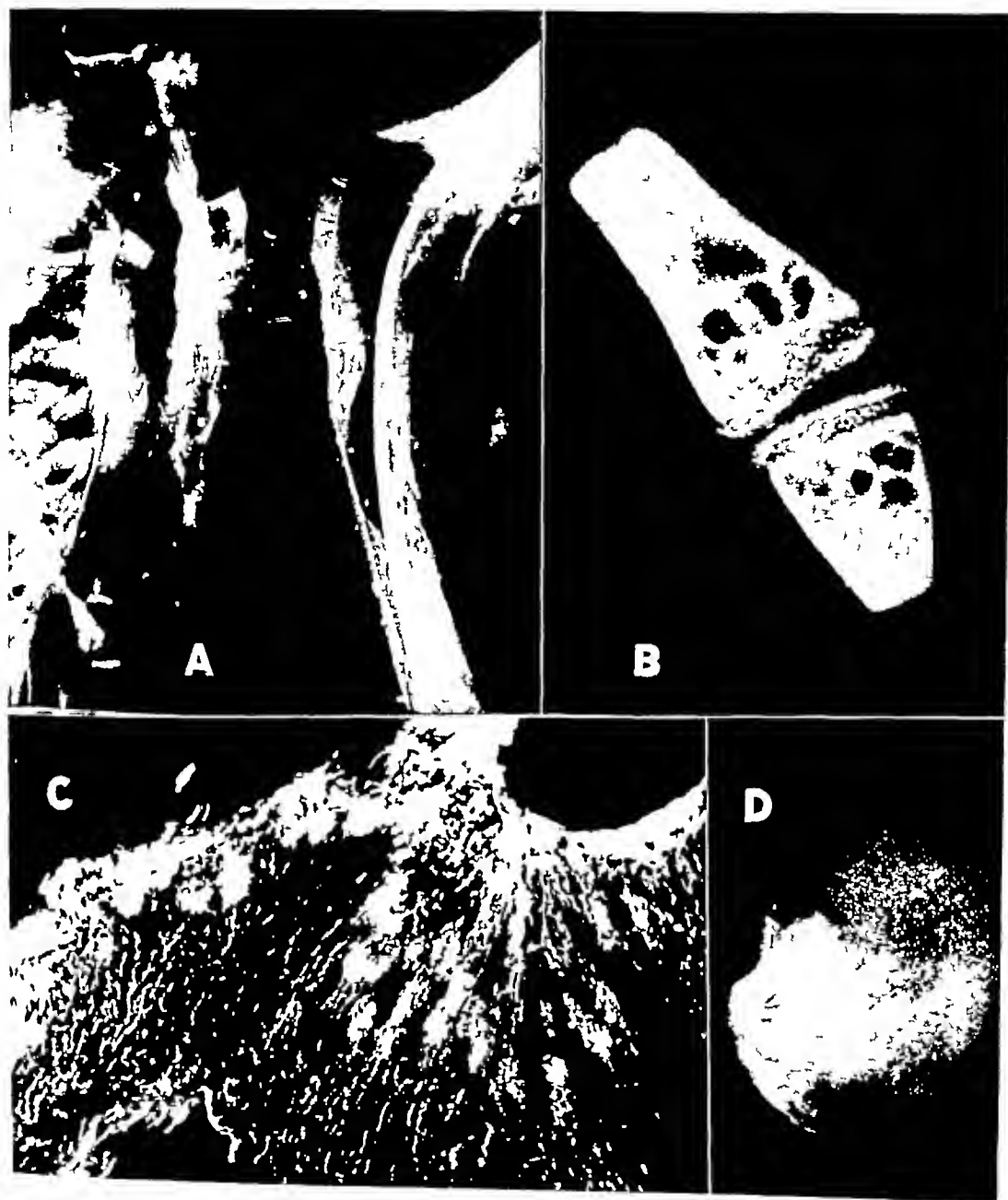


Fig 10 Monochromatic microradiographs $\times 150$ A Body of small sweat bee (spots are pollen caught on microscopic hairs) B Smallest bone in foot of very small frog C Thorotrast impregnated frog kidney D Circulation in embryonic bean of mercuric chloride solution

pine seeds, frogs, and the bones of the hands. For these last, monochromatic radiographs are also shown for copper, cobalt, and chromium characteristic radiations.

5 These new tests of monochromatic macroradiography are the result of ex-

perience with microradiography, in which images registered on fine-grained photographic emulsion are enlarged up to 400 diameters, and for which monochromatic beams are essential.

6 Multiple monochromatic microradiography is the result of choice of several

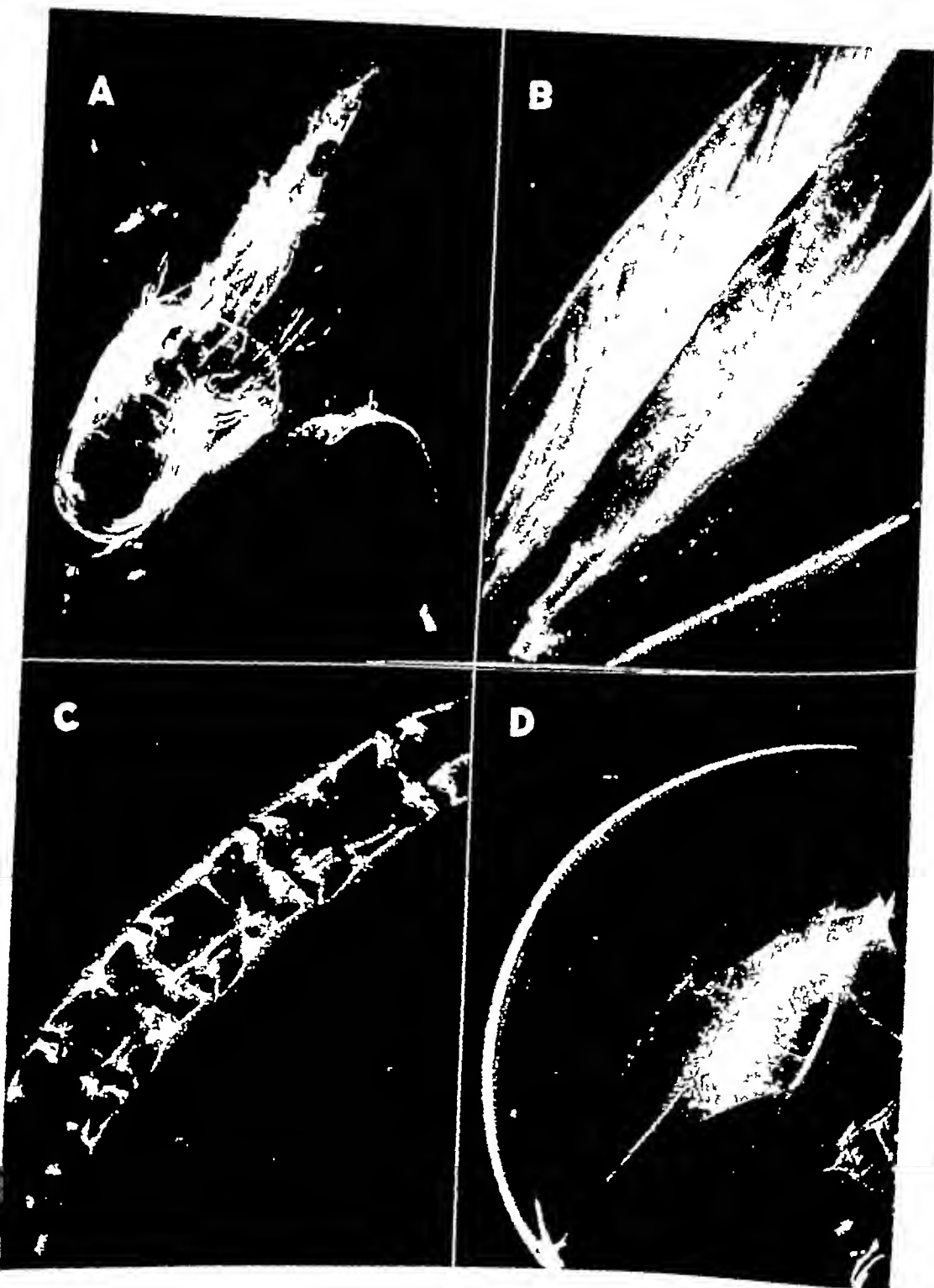


Fig 11 Monochromatic microradiographs of parts of common housefly $\times 150$ A Mouth C Antenna D Eye Wing

monochromatic rays from tubes with various targets

7 Microradiographs of several specimens of biological or medical interest are used to illustrate the three-dimensional details of structure

8 A plea is made for use of monochromatic radiation for special diagnostic problems and for research in roentgen-ray departments of hospitals and other institutions

ACKNOWLEDGMENT For indispensable assistance in formulation of ideas and technics, and for experimental tests which are still in progress, the writer acknowledges his great indebtedness to Mr A W Zimmerman, Fort Wayne, Ind, and W F Wagner, research assistant at the University of Illinois

Department of Chemistry
University of Illinois
Urbana, Ill

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- 2 ROGERS, T H Radiology 48 594, 1947

SUMARIO

Aplicaciones Médicas, Biológicas e Industriales de la Radiografía Monocromática y la Microrradiografía

1 Muéstrase el empleo, para el diagnóstico radiográfico en ciertos casos, de rayos X esencialmente monocromáticos, y especialmente de los dobles $K\alpha$ de un foco de molibdeno con un largo de onda de 0.71 \AA , comparándolos con la radiación de tungsteno generada a los mismos voltaje y corriente

2 A una distancia de 3 m, la dosis de los tubos de difracción obtenible en el comercio es mucho mayor que la de los tubos corrientes de diagnóstico

3 Demuéstrase experimentalmente la necesidad de calibrar la velocidad de las pantallas intensificadoras

4 En las radiografías monocromáticas obtiéndose una definición apreciablemente mayor de los detalles delicados Como ejemplos preséntanse finísimas grietas en impresiones, semillas, ranas y huesos de las manos Para los últimos también se presentan radiografías monocromáticas con típicas radiaciones de cobre, cobalto y cromo

5 Estos nuevos ensayos de la microrradiografía monocromática son consecuencia de las observaciones realizadas con la microrradiografía, en la cual se agrandan hasta 40 diámetros las imágenes registradas en emulsiones de granos finos, siendo indispensable para ella los rayos monocromáticos

6 La microrradiografía monocromática múltiple representa el resultado de la elección de varios rayos monocromáticos procedentes de tubos con varios focos

7 A fin de demostrar los pormenores en tres dimensiones de su composición, utilízanse microrradiografías de varios ejemplares de interés biológica o médica-mente

8 Abógase por el empleo de la radiación monocromática en ciertos problemas especiales de diagnóstico y para fines de investigación en los departamentos de roentgenología de los hospitales y otras instituciones

EDITORIAL

To the Members of the Radiological Society of North America

Historic Boston extends a most cordial welcome to the members, their families, and guests on the occasion of the Thirty-third Annual Meeting of the Radiological Society of North America at the Hotel Statler, Boston, November 30 to December 5, 1947

The scientific program and exhibits promise to fulfill the best traditions of the Society. The fruitful "refresher courses," original with this Society, remain as an integral part of the program. The commercial exhibits will be varied and embrace all the recent and projected developments in diagnostic and therapy apparatus.

An interesting Ladies' Program has been planned, comprising a tour of Boston including the Gardner Museum and a visit to Harvard College in Cambridge to see the world renowned collection of glass flowers.

Many of the historic places are within walking distance of the Society's hotel headquarters. Nearby is the State House showing the Bulfinch front, designed by Charles Bulfinch, considered one of the great architects of Colonial times. The dome of the State House, gilded in gold leaf, was painted gray during World War II, but has now been restored.

The Paul Revere House, 19 North Square, is the oldest house in the City of Boston. Built about 1660, it was purchased by Paul Revere in 1770 and there he resided until 1800. The immense fireplaces and ancient wall paper, and many other features of the Colonial period, make it a most interesting house to visit. It was restored in 1908.

The Old North Church, built in 1723, remains a classic in its lines. It was from the steeple of this church that the signal lanterns of Paul Revere were displayed

on April 18, 1775, which warned the country of the march of the British troops to Lexington and Concord.

Bunker Hill Monument occupies the spot on which one corner of the American redoubt at the Battle of Bunker Hill was located. The monument was begun in 1825 but remained unfinished until 1840, when its construction was recommenced largely through the efforts of American women. It is constructed of granite brought from the Quincy granite quarries by America's first steam railway.

Boston has not alone been first in things politic, but has pioneered in liberal education and medicine. Harvard College and the Massachusetts Institute of Technology are just across the Charles River. The Boston College group of buildings, at Chestnut Hill, is considered one of the finest examples of Gothic architecture in America.

Harvard Medical School and its classic marble lecture halls and laboratories are in Boston proper, surrounded by the Boston Lying-In Hospital, the Children's Hospital, and the Peter Bent Brigham Hospital. It was while a student at Harvard Medical School in 1898, that Dr. Walter Cannon made his classical observations on the movements of the stomach, using an opaque medium.

The New England Medical Center, the teaching unit of Tufts Medical College, is in down-town Boston and comprises the Boston Dispensary, the Floating Hospital for Children, the Pratt Diagnostic Center, and a new surgical building and medical school.

Boston University Medical School is in the South End of Boston with its own modern medical and surgical wings and the Evans Memorial Research laboratory.

The Boston City Hospital of 2,500 beds is close by and is used by all medical schools for teaching. Here is the Thorndike Memorial Laboratory for research, with Drs George Minot and William Castle directing. It was at the Boston City Hospital in 1896, only a year after Roentgen's discovery, that Dr Francis Williams began his unforgettable work in roentgen diagnosis, using a fluoroscope energized by a static machine which he had himself made.

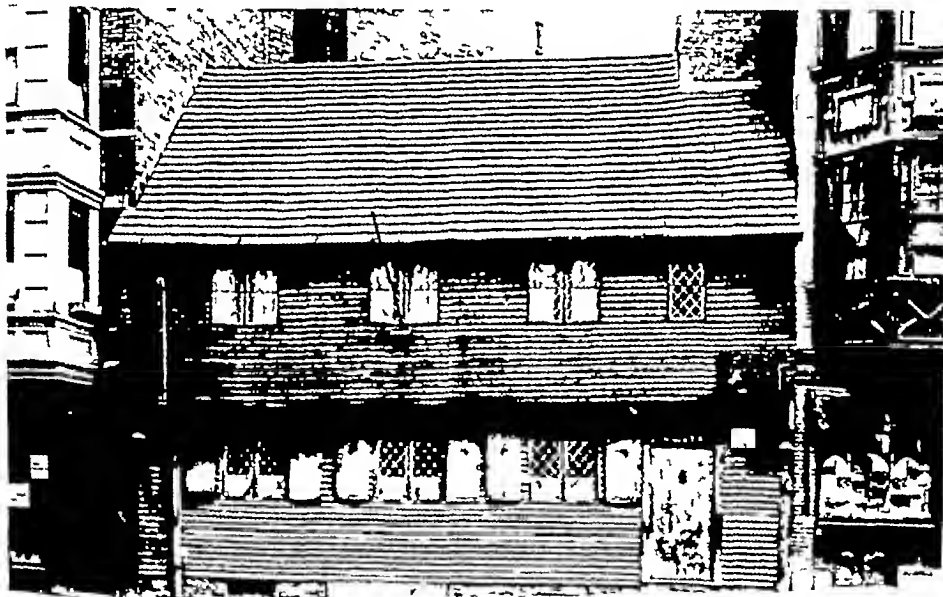
The Massachusetts General Hospital remains unique. Perhaps best known for the demonstration of Morton's discovery of ether, it has remained in the forefront of the great teaching hospitals of the world. Walter Dodd, the hospital phar-

macist, later to receive his medical degree from the University of Vermont and die a martyr to the cause, was first to interest himself in Roentgen's newly discovered rays. He was succeeded by Dr George W. Holmes, to whom so many students and radiologists in general owe so much.

All of these institutions are near by and will receive gladly any member of the R S N A. Anyone interested in any particular surgical operation will find all operations for the day posted at the Medical Library, 8 Fenway, which by the way houses many unusual incunabula.

Hotel accommodations will be adequate but reservations should be made early.

FREDERICK W. O'BRIEN, M.D.,
President



THE PAUL REVERE HOUSE

The Paul Revere House, 19 North Square is the oldest house in the City of Boston. It was built about 1660 and was purchased by Paul Revere in 1770. It was restored in 1908 and is open to the public on weekdays and holidays from 10 A.M. to 4 P.M.

RADIOLOGICAL SOCIETY OF NORTH AMERICA

THIRTY-THIRD ANNUAL MEETING, HOTEL STATLER, BOSTON
NOV 30-DEC 5, 1947

Sunday, November 30

PRELIMINARY PROGRAM

REGISTRATION

QUIZ PROGRAM

7 00 P M

Contestants JOHN D CAMP M D, L HENRY GARLAND, M D, FRED J HODGES, M D and LEO G RIGLER, M D

Referee MERRILL C SOSMAN, M D

Monday, December 1

GENERAL SESSION 10 30 A M

CALL TO ORDER

FREDERICK W O'BRIEN M D President
Boston, Mass

ADDRESS OF WELCOME

EDWARD F BAGG M D
President of Massachusetts Medical Society

PRESIDENTIAL ADDRESS

RADIOLOGY AND THE PRACTICE OF MEDICINE

FREDERICK W O'BRIEN M D

THE ECONOMICS OF MEDICINE (A SYMPOSIUM)

Chairman. Lowell S Goin, M.D

REV ALPHONSE SCHWITTALLA S J

DR MARJORIE SHEARON

MR. MAC F CAHAL Executive Secretary American
College of Radiology

COUNSELLORS' LUNCHEON 12 15 P M

DIAGNOSTIC SESSION 2 00 P M

- 1 An Analysis of X ray Findings in 405 Cases of Benign Gastric and Pyloric Ulcers WALTER A RUSSELL M D SIDNEY WEINTRAUB M D and HAROLD L TEMPLE M D New York Hospital New York N Y

- 2 Roentgenological Deformities of the Pyloric Portion of the Stomach with Absence of Surgical and Pathological Findings EDWARD L JENKINSON M D Chicago, Ill
- 3 X ray Observations Before and After Vagotomy, WARREN W FURRY M D, Chicago Ill
- 4 Spindle Cell Tumors of the Gastro Intestinal Tract WILLIAM L PALAZZO, M D and MILFORD D SCHULZ, M D, Massachusetts General Hospital Boston, Mass
- 5 The Significance of Gas in Hepatic Ducts WILLIAM J ELLIOT M D JAMES R LINGLEY M D, and JOHN F SHEEHAN, M D, Worcester Mass
- 6 Trichobezoar (Hair Ball) JOHN DAY PEAKE, M D, Mobile Ala

THERAPY SESSION 2 00 P M

- 1 Measurement of High Energy Neutrons G FAILLA PH D New York, N Y
- 2 Biological Effects of High Energy Neutrons, T C EVANS PH D New York, N Y
- 3 Protection from 1 and 2 Million Volt X rays C B BRAESTROP New York N Y
- 4 Distribution of Radioactive Isotopes by the Atomic Energy Commission and Some Medical Applications P C AEBERSOLD Oak Ridge, Tenn
- 5 Very High Energy Ionizing Radiations
- 6 Further Observations on the Use of Three Million Volt Roentgen Ray Therapy, RICHARD DRESSER M D Boston Mass
- 7 Physical Basis for the High Skin Tolerance of Supervoltage Roentgen Rays JOHN G TRUMP Sc D Massachusetts Institute of Technology Cambridge Mass
- 8 Concrete Protective Studies at Roentgen Ray Potentials of up to 1400 Kilovolts HAROLD O WICKOFF and LAURISTON S TAYLOR Washington D C

MEMBERSHIP DINNER AND EXECUTIVE SESSION 7 00 P M

Tuesday, December 2

DIAGNOSTIC SESSION 10 15 A M

- 1 Pulmonary Emphysema and Pulmonary Fibrosis Clinical Pathological and Roentgen Aspects DONALD S KING M D TRACY B MALLORY M D and LAURENCE L ROBBINS M D Massachusetts General Hospital Boston Mass
- 2 Milary Calcification of the Lungs HOWARD P DOUB M D Detroit Mich

- 3 Intratracheal Atomization in the Diagnosis and Treatment of Disease of the Respiratory Tract, PEDRO L FARIÑAS M D Havana, Cuba
- 4 The Pathogenesis of Bronchiectasis A Roentgen Contribution, FELIX G FLEISCHNER, M D, Boston Mass

THERAPY SESSION 10 30 A M

- 1 Roentgen Therapy of Carcinoma of the Lower Lip, J A DEL REGATO M D Columbia, Mo
- 2 Importance of X ray Examination in Cancer of the Larynx and Hypopharynx, FELIX E LEBORGNE, Montevideo Uruguay
- 3 Cancer of the Larynx Five Year Results of Concentration Radiotherapy, MAX CUTLER M D, Chicago, Ill
- 4 The Selection of the Treatment Method in Larynx Cancer, HAYES E MARTIN M D New York, N Y
- 5 Roentgen Therapy of Carcinoma of the Larynx Fifteen Years' Experience, WILLIAM HARRIS, M D RUDOLPH KRAMER, M D, and SIDNEY M SILVERSTONE, New York, N Y

EXECUTIVE SESSION 1 45 P M

Report of Nominating Committee

DIAGNOSTIC SESSION 2 30 P M

- 1 Some Considerations of the Roentgen Diagnosis of Silicosis and Conditions that May Simulate It EUGENE P PENDERGRASS M D, and AGRIPPA G ROBERT, M D, University of Pennsylvania, Philadelphia, Penna
- 2 Significance of Occupational History in the Diagnosis of Silicosis, THEODORE HATCH Industrial Hygiene Foundation Pittsburgh Penna
- 3 Anthraco-Silicosis WILLIAM J CORCORAN, M D Scranton, Penna
- 4 Pathogenesis of Industrial Pulmonary Disease, WILLARD F MACHLE M D New York, N Y
- 5 Further Observations of Lung Changes Associated with the Manufacture of Alumina Abrasives C G SHAVER M D St Catharines, Ontario, Canada
- 6 Delayed Pneumonitis of Unknown Origin Occurring in Workers with Fluorescent Powders STANLEY A WILSON M D Salem Mass

THERAPY SESSION 2 30 P M

- 1 Induction of Leukemia in Inbred Mice by X rays HARRY W MINER, M D and ARTHUR KIRSCHBAUM M D University of Minnesota Medical School Minneapolis Minn
- 2 The Practical Aspects of the Diagnosis Treatment and Prognosis of Hodgkin's Disease and Allied Disorders, HENRY JACKSON JR. M D Boston Mass
- 3 Pathologic Aspects of Lymphoid Tumors SHIELDS WARRIN, M D Boston Mass
- 4 Clinical Uses of Nitrogen Mustards LLOYD F CRAVER M D Memorial Hospital New York

- 5 The Newer Nitrogen Mustards in the Treatment of Leukemia, JOSEPH H BURCHENAL M D The Sloan-Kettering Institute for Cancer Research, New York, N Y
- 6 Pathological Changes Following the Use of Nitrogen Mustards, SOPHIE SPITZ, M D, New York
- 7 Orbital Lymphomas, MILFORD D SCHULZ, M D, and PARKER HEATH, M D, Massachusetts General Hospital Boston, Mass
- 8 Radiation Treatment of Lymphoid Tumors, HUGH F HARE, M D C F SORNBERGER, M D, and W C MULRY M D, Lahey Clinic, Boston, Mass

THE CARMAN LECTURE 8 00 P M

DOUGLAS QUICK M D
New York N Y

Wednesday, December 3

DIAGNOSTIC SESSION 10 15 A M

SYMPOSIUM ON PEDIATRIC ROENTGENOLOGY

RALPH S BROMER, M D, Philadelphia Children's Hospital, JOHN CAFFEY M D Babies Hospital, New York, DONALD L McRAE, M D, Montreal Children's Hospital, WILLIAM A EVANS, JR M D Detroit Children's Hospital and MARTIN H WITTENBORG M D Children's Hospital, Boston, Mass

THERAPY SESSION 10 15 A M

SYMPOSIUM ON RADIOACTIVE IODINE

- 1 Radioactive Iodine as a Tool in the Study of Thyroid Physiology RULON W RAWSON, M D, Massachusetts General Hospital Boston, Mass
- 2 Radioactive Iodine Studies of Functional Thyroid Carcinoma, VIRGINIA KNEBLAND FRANTZ M D, New York N Y
- 3 Factors Involved in the Experimental Therapy of Metastatic Thyroid Cancer with I¹³¹ A F HOCKER, M D and J B TRENNELL M D, New York
- 4 Treatment of Hyperthyroidism with Radioactive Iodine (8-day half life) EARLE M CHAPMAN M D Massachusetts General Hospital, Boston Mass
- 5 Clinical Experience in Diagnosis and Treatment of Toxic Goiter with Radioactive Iodine (8-day half life) SIDNEY C WERNER M D and EDITH H QUIMBY Sc D Columbia University, New York

DIAGNOSTIC SESSION 2 00 P M

- 1 Adult and Four Chamber Angiocardiography, GEORGE P ROBB M D, Washington, D C
- 2 Angiocardiography in Congenital Heart Disease, R A COOLEY M D H T BAHNSON, M D, and C R HANLON M D Johns Hopkins Hospital, Baltimore Md
- 3 Further Experience with the Right Heart Catheter in Congenital Heart Disease LEWIS DEXTER M D Peter Bent Brigham Hospital Boston Mass

- 4 Radiographic Demonstration of Anomalies of the Aorta and Great Vessels E B D NEUHAUSER, M D Children's Hospital Boston, Mass
- 5 Surgical Experience with Coarctation of the Aorta and Double Aortic Arch ROBERT E GROSS M D Children's Hospital, Boston, Mass
- 6 Cerebral Arteriography and Aneurysms of the Cerebral Arteries, JAMES L POPPEN, M D Lahey Clinic Boston, Mass
- 7 Venography of the Extremities GEORGE MIXTER, M D Massachusetts Memorial Hospital Boston, Mass
- 8 Scalloped Ribs Without Coarctation PHILIP BATCHELDER M D, and ROBERT J WILLIAMS, M D Providence, R I

THERAPY SESSION 2 00 P M

- 1 Roentgen Therapy of Carcinoma of the Vulva and Female Urethra FRANZ BUSCHKE M D and SIMON T CANTRIL M D Seattle Wash
- 2 Intracavitary Radium Therapy and the Immediate and Late Results in Cancer of the Cervix HARRY H BOWING, M D, Mayo Clinic, Rochester, Minn
- 3 The Treatment of Cancer of the Cervix Uteri by Intravaginal Roentgen Therapy GRAY H TWOMBLY M D New York, N Y
- 4 Review of Ten Years' Experience with Transvaginal Roentgen Therapy RALPH M CAULK M D Washington D C
- 5 External Deep X-ray Therapy An Adjunct in the Treatment of Carcinoma of the Cervix Uteri with the Long Interstitial Element Needles, GEORGE W WATERMAN M D Providence R I
- 6 Carcinoma of the Cervical Stump WILLIAM E COSTLOW M D Los Angeles Calif
- 7 Carcinoma of Cervix Uteri Improvement of Radiation Technic with Aid of Serial Biopsies and Million Volt Roentgen Therapy MILTON FRIEDMAN M D New York N Y
- 8 Future Probable Trends in the Irradiation Treatment of Carcinoma of the Cervix with a New Type of Expanding Cervical Colpostat Radium Application EDWIN C ERNST M D Barnard Free Skin and Cancer Hospital St Louis Mo

Thursday, December 4

DIAGNOSTIC SESSION 10 15 A M

- 1 The Effect of the Variations of the Nasal Sinuses on the Roentgenograms FRED W DIXON M D Cleveland Ohio
- 2 Clinical and Roentgenological Consideration of Nasal Sinus Conditions A S MACMILLAN M D and LEROY A SCHALL, M D Boston Mass
- 3 A Study of the Cervical Subarachnoid Space with Particular Reference to Arnold Chiari Malformation and Syringomyelia JOSEPH H MARKS M D and KENNETH E LIVINGSTON M D Boston Mass

- 4 Intraventricular Epidermoid HARRY HAUSER, M D, and CHARLES W ELKINS M D Cleveland Ohio
- 5 The Diagnosis and Treatment of Medulloblastoma, CARLETON B PEIRCE, M D and WILLIAM A CONE M D Montreal, Canada

THERAPY SESSION 10 15 A M

- 1 The Treatment of Multiple Myeloma L HENRY GARLAND, M D San Francisco, Calif
- 2 Hormonal Studies in Breast Cancer, IRA T NATHANSON M D Boston Mass
- 3 The Treatment of Breast Cancer Metastatic to Bone with Testosterone FRANK E ADAIR M D New York N Y
- 4 Clinical Manifestations of Pituitary Disease LEWIS M HURATHAL M D Boston, Mass
- 5 Diagnosis and Treatment of Pineal Tumors GILBERT HORRAX M D Boston Mass

EXECUTIVE SESSION 1 45 P M

Election of Officers

DIAGNOSTIC SESSION 2 00 P M

- 1 Roentgen Evaluation of Hip Lesions in Infancy and Childhood Based on Experience at Newington Home for Crippled Children, GILBERT W HEUBLEIN, M D, LOUIS BERNSTEIN, M D and B J HUBENET M D Hartford Conn
- 2 Eosinophilic Granuloma and Xanthomatosis WILLIAM T GREEN M D Boston Mass
- 3 Eosinophilic Granuloma and Xanthomatosis SYDNEY FARRER, M D, Boston, Mass
- 4 The Osseous Manifestations of Neurofibromatosis With Special Reference to Lesions of the Ribs, JOHN F HOLT M D and EDWIN M WRIGHT, M D Ann Arbor, Mich
- 5 Sickle-cell Anemia in Adults with Osseous and Visceral Manifestations, ROBERT P BALL M D, and OMAR K LEGANT M D Presbyterian Hospital New York N Y
- 6 Polyostotic Fibrous Dysplasia (Albright's Syndrome) and Its Comparison with Chondroplasia (Ollier's Disease) A Correlation of the Pathological and Radiological Findings L R SANTE M D, WILLIAM BAUER M D and R M O'BRIEN M D, St Louis Mo
- 7 Meningocele Within the Sacrum W ARCHER M D GEORGE COOPER JR M D and R R, HOFFMAN M D University Va

THERAPY SESSION 2 00 P M

- 1 Roentgen ray Treatment of Bacteraemia Carbonosa Infections MANUEL RIEBELING M D Guadalajara Mexico
- 2 Radiation Therapy of Thrombophlebitis JOHN S BOUSLOG M D Denver Colo

- 3 Radiation Treatment of Hemangiomas, ROBERT B TAFT, M D Charleston, S C
- 4 Roentgen Ray Treatment of Severe Asthma, E T LEDDY M D, Mayo Clinic, Rochester, Minn
- 5 Radiation Necrosis of the Jaw, ERNEST M DALAND, M D Boston Mass
- 6 The Use of X rays in the Prevention and Treatment of Infections JAMES F KELLY, M D, D A DOWELL M D, and JOHN E DOWNING, M D Omaha Nebr

ANNUAL BANQUET 7 00 P M

Friday, December 5

GENERAL SESSION 10 15 A M

- 1 The Roentgenologic Examination as an Aid in Diagnosis of Malignant and Potentially Malignant Lesions of the Large Bowel, JOSEPH C BELL, M D and JAMES B DOUGLAS M D, Louisville, Ky
- 2 Radiological Aspect of Amebic Colitis, J J VALLARINO, M D, Washington, D C
- 3 Large Lymphoid Cell Collections in the Mucosa of the Terminal Ileum Its Effect on Barium Shadows JOSEPHINE S WELLS M D, New York, N Y
- 4 Acute Small Intestinal Obstruction, IRA LOCKWOOD, M D ARTHUR B SMITH M D and JOHN W WALKER, M D, Research Clinic Kansas City Mo
- 5 Extrinsic Deformities of the Colon ROBERT C PENDERGRASS M D Americus Ga

- 6 Barium Sulfate in Saline Suspension Examination of the Left Colon in the Presence of Partial Obstruction, GEORGE M WYATT, M D Washington, D C

GENERAL SESSION 2 00 P M

- 1 Arthrograms HAMPAR KELIKIAN M D and ELBERT K LEWIS, M D, Chicago, Ill
- 2 Chronic Idiopathic Hypertrophic Osteoarthropathy, JOHN D CAMP, M D, and ROBERT L SCANLAN, M D, Mayo Clinic Rochester Minn
- 3 Contact Therapy in Treatment of Superficial Lesions, W S ALTMAN M D Quincy Mass, B LEVINE M D, and H F FRIEDMAN M D Boston Mass
- 4 Prenatal Estimation of Birth Weight by Pelviccephalometry, S W DONALDSON M D, and WILLIAM D CHENEY, M D Ann Arbor, Mich
- 5 Hydronephrosis A Radiological Classification Based on Anatomical Variations SAMUEL A ROBINS, M D and JOSEPH FISCHMAN M D, Boston Mass
- 6 A Study of the Hands of Radiologists, MARGARET NICKSON, Argonne National Laboratory, Chicago Ill
- 7 Rotation Therapy, SIDNEY J HAWLEY M D Seattle Wash
- 8 Treatment of Deep-Seated Malignant Growths with Multiple Port Technic Simulating Rotation Therapy IRA I KAPLAN M D, and S I ETKIN M D, Bellevue Hospital, New York



ANNOUNCEMENTS AND BOOK REVIEWS

ANNUAL MEETING, RADIOLOGICAL SOCIETY OF NORTH AMERICA

As everyone must know by now, the Thirty-Third Annual Meeting of the Radiological Society of North America will be held in Boston, Nov 30 to Dec 5, with headquarters at the Hotel Statler

The program of Refresher Courses, which will begin on Sunday, Nov 30, was included in RADIOLOGY for September. The Scientific Program appears elsewhere in this issue

The Women's Committee has prepared a very interesting program for the lady guests and is anxious to contact as many of the women as possible so that they will know how many are going to attend

On Monday, Dec 1, a breakfast at 10 00 A M at the Women's City Club, 39 Beacon St., followed by a book review by Alice Dickson Bond, is planned. On Tuesday there will be a concert and tour of Mrs Jack Gardner's palace, with transportation provided, and Wednesday a tour of historic Boston lasting three and one half hours

The ladies are requested to take notice of the special program planned for them at the Boston meeting

AMERICAN MEDICAL ASSOCIATION SECTION ON RADIOLOGY

The American Medical Association will hold its 1948 annual session in Chicago, June 21-25. Those who wish to present papers before the Section on Radiology should communicate with the secretary, Dr U V Portmann, 2020 E 93rd St., Cleveland 6 Ohio, before Dec 1 1947

AMERICAN COLLEGE OF RADIOLOGY

New officers elected at the 24th annual meeting of the American College of Radiology are E C Ernst, M D, St Louis, President, to succeed E H Skinner, M D, Kansas City. Charles L Martin, M D, Dallas, Vice-President, Warren Furey, M D, Chicago, Treasurer. Lewis G Allen, M D, Kansas City, Kan., was elected to the Board of Chancellors, and E P Pendergrass, M D, Philadelphia, was re-elected as Chairman of the Board of Chancellors

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

Over 165 registered for the meeting of the Rocky Mountain Radiological Society in Denver, Aug 7-9. Among the guest speakers were Dr Lloyd Craver, Dr Kenneth Corrigan, Dr Eldwin Witwer

Dr Claude Hunt, Dr Leo Rigler, Dr Lowell Goin, and Dr Edgar McNamee.

The following officers were elected for the ensuing year: Dr James P Kirby, Salt Lake City, President, Dr Howard B Hunt, Omaha, Nebr., President elect, Dr Q B Coray, Salt Lake City, 1st Vice-President, Dr E M Hayden, Tucson, Ariz., 2d Vice-President, Dr John Bouslog, Denver, Colo., Historian, Dr M D Frazer, Lincoln, Nebr., Secretary-Treasurer

The next annual meeting of the Society will be held in Salt Lake City

A NEW ITALIAN JOURNAL OF RADIOLOGY

There have recently been received in the editorial offices of RADIOLOGY issues of a new Italian journal *Radiologia*, under the editorship of Professor Eugenio Milani, Director of the Instituto di Radiologia Medica, University of Rome. Dr Milani is interested in receiving articles for publication from American radiologists and asks that such contributions be addressed to him at Instituto di Radiologia Medica dell'Università di Roma, Policlinico Umberto I, Roma

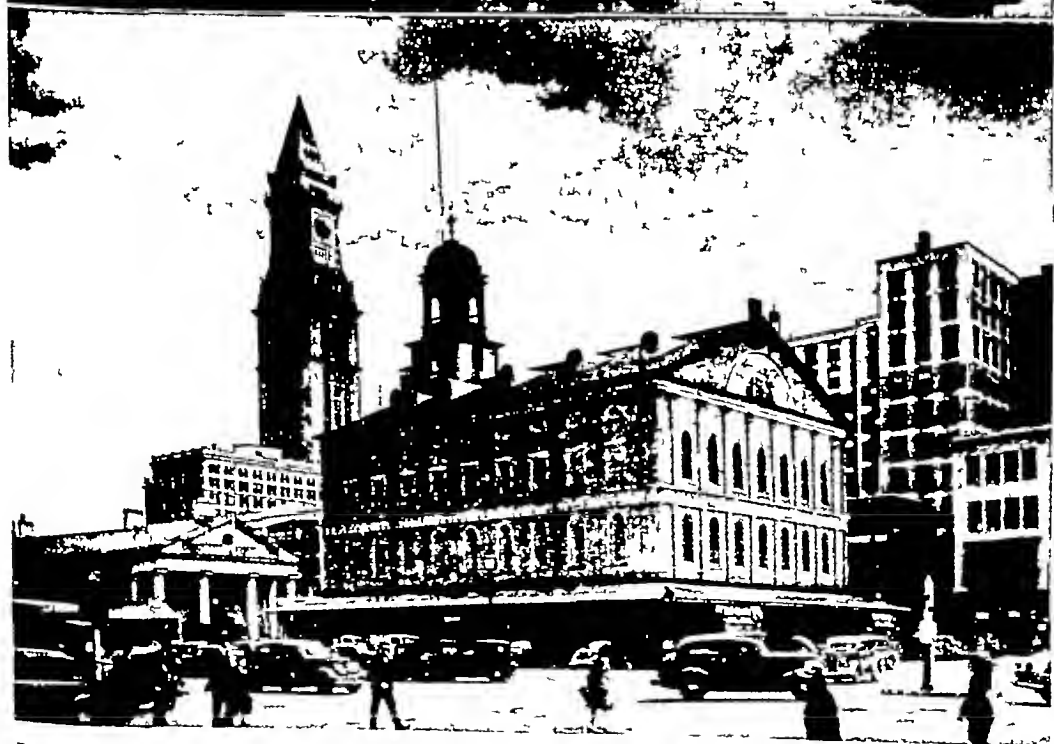
In Memoriam

HAROLD BENJAMIN THOMPSON, M D 1883-1947

Harold Benjamin Thompson, M D, of Seattle, Washington, one of the early radiologists of the Pacific Northwest, succumbed to coronary thrombosis on June 16 1947 after practicing his specialty for thirty five years

Dr Thompson was born in Appleton, Wisconsin, in 1883. He graduated from Rush Medical College in 1908. His interest in radiology appeared early in his career. While still a medical student he worked in the incipient department of radiology at Cook County Hospital. He started general practice in Seattle in 1909 and after 1912 limited his practice to radiology. He was radiologist to the Seattle General Hospital from 1915 to 1946 and during the same period was consultant in radiology at the Children's Orthopedic Hospital

Dr Thompson was a Fellow of the American College of Radiology and a member of the Radiological Society of North America, the Washington State Radiological Society, and the Pacific Northwest Radiological Society. His wide experience and keen ability at observation and diagnosis won him the respect of all his colleagues. His death marks not only the loss of a pioneer in radiology, but a wise counsellor and sincere friend to the profession of medicine



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RADIOLOGICAL SOCIETIES SECRETARIES AND MEETING DATES

Editor's Note Secretaries of state and local radiological societies are requested to cooperate in keeping this up-to-date by notifying the editor promptly of changes in officers and meeting dates Address Howard H. M D, The Henry Ford Hospital, Detroit 2, Mich

UNITED STATES

RADIOLOGICAL SOCIETY OF NORTH AMERICA *Secretary-Treasurer*, Donald S Childs, M D, 607 Cal Arts Bldg, Syracuse 2, N Y

RADIUM SOCIETY *Secretary* Hugh F Hare, 605 Commonwealth Ave. Boston 15, Mass

ROENTGEN RAY SOCIETY *Secretary*, Harold Kerr, M D Iowa City Iowa

COLLEGE OF RADIOLOGY *Secretary*, Mac F Von Wacker Dr Chicago 6, Ill

RADIOLOGY A M A *Secretary*, U V M D, Cleveland Clinic, Cleveland 6,

RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Suckley M D, Bell Bldg Montgomery meeting at the time and place of the State Medical Association meeting

RADIOLOGICAL SOCIETY *Secretary*, Fred Pine Bluff Meets every three annually at meeting of State Medical

ASSOCIATION SECTION ON RADIOLOGY, Sydney F Thomas M D Palo Alto

STATE MEDICAL ASSOCIATION, RADIOLOGY *Secretary* Morris Horwitz 1000 Broadway Blvd Los Angeles 5 Meets every 1st of each month at County

SOCIETY *Secretary* L Henry Sutter St San Francisco 8 State Medical Association SOCIETY *Secretary* R F 1 Fourth Ave San Diego every 1st of each month

SAN FRANCISCO *Secretary* 2000 Van Ness Ave Meets 1st Thursday at 7 45 P M McNe Hall, Stanford University to December at Toland Memorial Hospital

Secretary, Washington Hospital 1619 Milwaukee St Friday of each month Medicine and Hospitals

Connecticut

CONNECTICUT STATE MEDICAL SOCIETY SECTION ON RADIOLOGY *Secretary*, Robert M Lowman M D, Grace New Haven Hospital, Grace Unit New Haven Meetings bimonthly, second Thursday

Florida

FLORIDA RADIOLOGICAL SOCIETY *Secretary-Treasurer*, J A Beals M D, St Luke's Hospital, Jacksonville Meets semiannually, in April preceding the annual meeting of the Florida Medical Society, and in November

Georgia

GEORGIA RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Robert Drane, M D De Renne Apartments, Savannah Meets in November and at the annual meeting of State Medical Association

Illinois

CHICAGO ROENTGEN SOCIETY *Secretary*, T J Wachowski, M D, 310 Ellis Ave Wheaton Meets at the Palmer House, second Thursday of October, November, January, February, March, and April, at 8 00 P M

ILLINOIS RADIOLOGICAL SOCIETY *Secretary-Treasurer*, William DeHollander, M D, St Johns' Hospital, Springfield Meetings quarterly as announced

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY *Secretary*, Frank S Hussey, M D 250 East Superior St Chicago 11

Indiana

INDIANA ROENTGEN SOCIETY *Secretary-Treasurer*, J A Campbell, M D, Indiana University Hospitals, Indianapolis 7 Annual meeting in May

Iowa

IOWA X-RAY CLUB *Secretary* Arthur W Erskine, M D, 326 Higley Building, Cedar Rapids Meets during annual session of State Medical Society

Kentucky

KENTUCKY RADIOLOGICAL SOCIETY *Secretary-Treasurer* Sydney E Johnson M D 101 W Chestnut St, Louisville

LOUISVILLE RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Everett L Pirkey, Louisville General Hospital Louisville 2 Meets second Friday of each month at Louisville General Hospital

Louisiana

LOUISIANA RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Johnson R Anderson M D No Louisiana Sanitarium Shreveport Meets with State Medical Society

Surviving Dr Thompson are his wife, Mrs Phoebe Howe Thompson, a daughter, and a son, Dr William H Thompson, at present completing his post graduate study in radiology

SYDNEY J HAWLEY, M D

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits

PRACTICAL X-RAY TREATMENT By ARTHUR W ERSKINE, M D. A volume of 155 pages with 22 illustrations. Published by The Bruce Publishing Company, St Paul and Minneapolis, 3d edition, 1947

AN INTRODUCTION TO BIOCHEMISTRY By WILLIAM ROBERT FEARON, M A, Sc D, M B, Fellow of Trinity College, and Professor of Biochemistry, University of Dublin. Fellow of the Royal Institute of Chemistry. Member of the Royal Irish Academy. A volume of 569 pages. Published by Grune & Stratton, New York, 3d edition, 1947. Price \$6 00

ELECTRONICS AND THEIR APPLICATION IN INDUSTRY AND RESEARCH Edited by BERNARD LOVELL, O B E, B Sc, Ph D, F INST P, Physical Laboratories, University of Manchester. A volume of 660 pages, with 404 illustrations. Published by the Pilot Press, Ltd, London, 1947. Price 42s, net

Book Reviews

REPORT OF THE CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE, MANCHESTER, 1946

This report of the Christie Hospital and Holt Radium Institute, Withington, Manchester, for 1946, contains a number of interesting photographs of buildings and equipment, and full financial details, and as usual an interesting analysis of the cancer material treated by the Institute.

The types of tumors classified according to localization, whether primary or secondary, and whether previously treated in other institutions together with details of the sites, are listed, and the geographical origin of the patients is given,

showing that some have come from as far away as the Barbadoes and South Africa.

A summary shows that the work done has doubled since 1938. New patients for 1946 number nearly 6,000, and the total number of treatments has reached approximately 7,000.

Unfortunately, the shortage of paper and lack of free funds have prevented the publication of details of treatment but the report reflects, as in the past, a very large amount of work accomplished and shows extremely valuable co-ordination with nearby institutions in diagnosis and treatment. Now that the War is over we may look forward next year to a fuller record of the work of this remarkable institution by its medical and research staff, headed by the world famous director, Ralston Paterson.

LA RADIOTERAPIA EN CLÍNICA. ELEMENTOS DE FÍSICA, BIOLOGÍA Y TERAPÉUTICA [Clinical Radiotherapy. The Physical and Biological foundations of the Roentgen and Becquerel Curie rays]. By PROF DR. ALFONSO C FRANGELLA, Sub-Director de Instituto de Radiología de la Facultad de Medicina, Montevideo. Montevideo, 'Impresora Uruguaya,' S A, 1942. A volume of 883 pages with 427 illustrations.

This monumental volume of nearly nine hundred pages is well printed, well illustrated, and well arranged, constituting a fountain of information relative to clinical radiotherapy. Tribute is paid to Professor Doctor Pedro A Barcia and the late Professor Doctor Carlos Butler, and other Uruguayan pioneers.

After a prologue by Professor José A Saralegui, the author devotes 285 pages to the physics of roentgen and radium therapy. In harmony with the widespread feeling among our Latin American neighbors that x-rays and radium really should be referred to as the rays of Roentgen and Becquerel-Curie, this terminology is followed throughout the work. The publication of this book antedates the epoch making discoveries regarding radiation which became public following the use of the atom bomb.

The second part of the work consists of about one hundred pages, relates to radiobiology and summarizes our knowledge of the effect of Roentgen and Becquerel-Curie rays on living matter and especially on the human organism. The remainder of the book includes the clinical therapeutic indications and dosages of x-ray and radium therapy. Numerous illustrations some in color, illuminate the text. The language is direct, dignified, and a real treat to readers of Spanish.

Oregon

OREGON RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Wm Y Burton, M D, 242 Medical Arts Bldg, Portland 5 Meets monthly, on the second Wednesday, at 8 00 P M in the library of the University of Oregon Medical School

Pacific Northwest

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Sydney J Hawley, M D, 1320 Madison St, Seattle 4, Wash Meets annually in May

Pennsylvania

PENNSYLVANIA RADIOLOGICAL SOCIETY *Secretary-Treasurer* James M Converse M D 416 Pine St Williamsport 8 Meets annually

PHILADELPHIA ROENTGEN RAY SOCIETY *Secretary* Calvin L Stewart, M D, Jefferson Hospital, Philadelphia 7 Meets first Thursday of each month at 8 00 P M, from October to May in Thomson Hall, College of Physicians, 21 S 22d St

PITTSBURGH ROENTGEN SOCIETY *Secretary-Treasurer*, Lester M J Freedman, M D, 415 Highland Bldg, Pittsburgh 6 Meets second Wednesday of each month at 6 30 P M October to May inclusive

Rocky Mountain States

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Maurice D Frazer, M D, Lincoln Clinic, Lincoln Nebr

South Carolina

SOUTH CAROLINA X-RAY SOCIETY *Secretary-Treasurer*, Robert B Tift, M D, 103 Rutledge Ave, Charleston 16

Tennessee

MEMPHIS ROENTGEN CLUB Meetings second Tuesday of each month at University Center

TENNESSEE RADIOLOGICAL SOCIETY *Secretary-Treasurer*, J Marsh Frère M D, 707 Walnut St Chattanooga Meets annually with State Medical Society in April

Texas

DALLAS FORT WORTH ROENTGEN STUDY CLUB *Secretary* R Hyde M D Medical Arts Bldg, Fort Worth 2 Meetings on third Monday of each month in Dallas in the odd months and in Fort Worth in the even months

TEXAS RADIOLOGICAL SOCIETY *Secretary-Treasurer*, R P O Bannon M D 650 Fifth Ave Fort Worth 4 Next meeting Jan 17 1948

Utah

UTAH STATE RADIOLOGICAL SOCIETY *Secretary-Treasurer*, M Lowry Allen, M D, Judge Bldg, Salt Lake City 1 Meets third Wednesday, January, March, May, September, November

UNIVERSITY OF UTAH RADIOLOGICAL CONFERENCE *Secretary*, Henry H Lerner, M D Meets first and third Thursdays, September to June, inclusive, at Salt Lake County General Hospital

Virginia

VIRGINIA RADIOLOGICAL SOCIETY *Secretary*, E Latan Flanagan, M D, 215 Medical Arts Bldg, Richmond 19

Washington

WASHINGTON STATE RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Homer V Hartzell, M D, 310 Stimson Bldg, Seattle 1 Meetings fourth Monday October through May, at College Club, Seattle

Wisconsin

MILWAUKEE ROENTGEN RAY SOCIETY *Secretary-Treasurer*, C A H Fortier M D 231 W Wisconsin Ave, Milwaukee 3 Meets monthly on second Monday at the University Club

RADIOLOGICAL SECTION OF THE WISCONSIN STATE MEDICAL SOCIETY *Secretary*, S R Beatty, M D, 185 Hazel St Oshkosh Two-day meeting in May and one day at annual meeting of State Medical Society in September

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE Meets first and third Thursdays 4 to 5 P M, September to May, inclusive, Room 301 Service Memorial Institute, 426 N Charter St, Madison 6

CANADA

CANADIAN ASSOCIATION OF RADIOLOGISTS *Honorary Secretary-Treasurer*, E M Crawford, M D, 2100 Marlowe Ave., Montreal 28, Quebec Meetings in January and June

LA SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES *General Secretary*, Origène Dufresne, M D, Institut du Radium, Montreal Meets on third Saturday of each month

CUBA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA Offices in Hospital Mercedes, Havana Meets monthly

MEXICO

SOCIEDAD MEXICANA DE RADIOLOGÍA Y FISIOTERAPIA *General Secretary*, Dr Dionisio Pérez Cosío, Marsella 11, México, D F Meetings first Monday of each month

ORLEANS PARISH RADIOLOGICAL SOCIETY *Secretary*, Joseph V Schlosser, M D, Charity Hospital of Louisiana, New Orleans 13 Meets first Tuesday of each month

SHERBROOK RADIOLOGICAL CLUB *Secretary*, Oscar O Jones, M D, 2622 Greenwood Road Meets monthly September to May, third Wednesday, 7 30 P M

Maryland

BALTIMORE CITY MEDICAL SOCIETY, RADIOLOGICAL SECTION *Secretary*, Harry A Miller 2452 Eutaw Place, Baltimore

Michigan

DETROIT X-RAY AND RADIUM SOCIETY *Secretary Treasurer*, E R Witwer, M D, Harper Hospital, Detroit 1 Meetings first Thursday of each month from October to May, at Wayne County Medical Society club rooms

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS *Secretary Treasurer*, R B MacDuff, M D, 220 Genesee Bank Building Flint 3

Minnesota

MINNESOTA RADIOLOGICAL SOCIETY *Secretary*, C N Borman M D 802 Medical Arts Bldg, Minneapolis 2 Regular meetings in the Spring and Fall

Missouri

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY *Secretary* John W Walker, M D, 306 E 12th St., Kansas City Mo Meetings last Friday of each month.

ST LOUIS SOCIETY OF RADIOLOGISTS *Secretary*, Edwin C Ernst, M D, 100 Beaumont Medical Bldg Meets on fourth Wednesday of each month, October to May

Nebraska

NEBRASKA RADIOLOGICAL SOCIETY *Secretary-Treasurer* O A Neely M D, 924 Sharp Building Lincoln Meetings third Wednesday of each month at 6 P M in either Omaha or Lincoln

New England

NEW ENGLAND ROENTGEN RAY SOCIETY *Secretary-Treasurer* George Levene, M D Massachusetts Memorial Hospitals Boston, Mass Meets monthly on third Friday at Boston Medical Library

New Hampshire

NEW HAMPSHIRE ROENTGEN SOCIETY *Secretary-Treasurer*, Albert C Johnston M D Elliot Community Hospital Keene. Meetings quarterly in Concord

New Jersey

RADIOLOGICAL SOCIETY OF NEW JERSEY *Secretary*, Raphael Pomeranz M D 31 Lincoln Park Newark 2 Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called

New York

ASSOCIATED RADIOLOGISTS OF NEW YORK, INC *Secretary*, William J Francis M D, East Rockaway, L I

BROOKLYN ROENTGEN RAY SOCIETY *Secretary Treasurer*, Abraham H Levy M D 1354 Carroll St, Bklyn 13 Meets fourth Tuesday of every month, October to April

BUFFALO RADIOLOGICAL SOCIETY *Secretary-Treasurer* Mario C Gian, M D, 810 Niagara St, Buffalo 1 Meetings second Monday evening each month October to May, inclusive

CENTRAL NEW YORK ROENTGEN SOCIETY *Secretary-Treasurer*, Dwight V Needham M D, 608 E Genesee St, Syracuse 10 Meetings in January, May, and October

LONG ISLAND RADIOLOGICAL SOCIETY *Secretary*, Marcus Wiener, M D, 1430 48th St, Brooklyn 19 Meetings fourth Thursday evening each month at Kings County Medical Bldg

NEW YORK ROENTGEN SOCIETY *Secretary* Wm Snow, M D, 941 Park Ave., New York 28

ROCHESTER ROENTGEN-RAY SOCIETY *Secretary*, Murray P George, M D, 280 Crittenden Blvd, Rochester 7 Meets at Strong Memorial Hospital third Monday September through May

North Carolina

RADIOLOGICAL SOCIETY OF NORTH CAROLINA *Secretary Treasurer*, James E Hemphill, M D Professional Bldg, Charlotte 2 Meets in May and October

North Dakota

NORTH DAKOTA RADIOLOGICAL SOCIETY *Secretary* Charles Heilman M D, 1338 Second St, N, Fargo

Ohio

OHIO RADIOLOGICAL SOCIETY *Secretary*, Carroll Dundon M D 1030 Reibold Bldg, Dayton 2 Next meeting at annual meeting of the Ohio State Medical Association May 1948

CENTRAL OHIO RADIOLOGICAL SOCIETY *Secretary*, Hugh A Baldwin, M D 347 E State St, Columbus

CINCINNATI RADIOLOGICAL SOCIETY *Secretary*, Eugene L Saenger, M D, 735 Doctors Bldg Cincinnati 2. Meets last Monday of the month September to May

CLEVELAND RADIOLOGICAL SOCIETY *Secretary Treasurer* George L Sackett, M D, 10515 Carnegie Ave, Cleveland 6 Meetings at 8 30 P M on fourth Monday October to April inclusive.

Oklahoma

OKLAHOMA STATE RADIOLOGICAL SOCIETY *Secretary-Treasurer* Peter M Russo M D 230 Osler Building Oklahoma City Meetings three times a year

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Considering the technical difficulties involved, the laminagrams are surprisingly good

CESARE GIANTURCO, M D

Establishment and Use of Fundamental Procedures in Tuberculosis Control. J A. Myers Pub Health Rep 61 1563-1583 Nov 1, 1946

This article represents the fruits of twenty-six years observation on tuberculosis in the city of Minneapolis. It shows the result of carefully planned long-term studies which have to be undertaken to evaluate such a chronic disease as tuberculosis. An example of the scrupulously careful work which the author and his cohorts have done is reflected by the tuberculin surveys made in the grade schools. In 1926 47.3 per cent reacted positively to tuberculin whereas in 1944 only 7.7 per cent were reactors. Also the attack rate among six year old children was reduced from 3.5 per cent in 1926 to 0.33 per cent in 1944.

The application of x-rays to the diagnosis of tuberculosis has undergone numerous changes in the period covered by the report. The adoption of paper film and its application to the photofluorographic technique have solved a problem that at first appeared unsurmountable. In the earlier years there was a considerable discrepancy between the findings on x ray examination and tuberculin testing, so that two questions arose. Why do so many tuberculin reactors present no evidence of calcification? and Why is so much evidence of calcification reported among non reactors to tuberculin? In answer to the first it is pointed out that the foci may be so small as to cast no shadow on the x ray film or they may be in some part of the chest not readily accessible to x ray inspection. A partial answer to the second question lies in the possibility that the interpretation is not correct in all cases. The calcification may be due to other causes than tuberculosis, and a tuberculous lesion resulting in calcification may become completely healed and sterilized so as to give no evidence of infection by the tuberculin test. In 1927 McPhedran showed that certain vascular shadows were frequently misinterpreted as calcium deposits and in 1930 all the films obtained up to that date were reinterpreted on this basis.

It was found after ten years that x ray inspection of the chest rarely revealed evidence of significant disease in children under twelve or fourteen years of age even though they reacted positively to tuberculin so that roentgen studies in this group were discontinued. The use of stereoscopic films was also discontinued after 1931 since it was found that no significant disease could be detected on one film of a stereoscopic pair that was not equally discernible on the other.

The ten year data also revealed that no phase of the examination had resulted in the discovery of a single proved case of tuberculosis among non reactors to tuberculin. From 1921 to 1941 5968 children who were non reactors to tuberculin were observed. In 95.6 per cent evidence of disease of any kind was detected by x ray film of the chest. In the remaining 4.4 per cent there was only evidence of pleural changes, calcium deposits and non tuberculous pulmonary disease. Among 4377 reactors on the other hand only 58.1 per cent had films that were entirely clear. The remaining 41.9 per cent gave evidence of pleural changes, primary lesions in the pneumonic or atelectatic stage, calcification, non tuberculous pulmonary disease and pulmonary tuberculosis of the reinfection type. For this reason chest x ray examinations of non reactors were discontinued.

Between 1921 and 1926, 1033 children who were reactors were observed. Fifteen at the average age of fourteen years showed evidence of reinfection type pulmonary tuberculosis. Nine of these died at the average age of twenty. By 1941 41 other cases of pulmonary tuberculosis of the reinfection type were seen with 14 deaths at an average age of twenty-two. It is thus obvious that a positive tuberculin reaction in childhood makes mandatory a long and careful follow up with x rays. In spite of the great value of x rays it is strongly recommended that no one—roentgenologist, pediatric internist, surgeon or chest specialist—attempt to diagnose any pulmonary pathologic condition by x ray while to attempt to determine the activity of tuberculous lesions by a single x ray shadow is preposterous. There are but two ways to diagnose tuberculosis: (1) the finding and identification of the tubercle bacillus and (2) the tuberculin reaction.

Of the many persons observed in the Minneapolis work more than 1000 adults—mostly students of nursing and medicine—have developed primary tuberculosis while under observation. They have tolerated the first infection type of tuberculosis as well as have those infected in childhood, and moreover, they have not developed subsequently significant chronic reinfection type of tuberculosis to a greater degree than have those who entered the observation group as tuberculin reactors. The theory propounded in 1920, therefore—that a first infection postponed to adulthood is exceedingly hazardous—is untenable.

When shadows of lesions which were thought to be tuberculous were seen in children and young adults who were apparently in excellent health and presented no other symptoms other than a positive tuberculin reaction it was assumed that the majority of these lesions represented clinical disease that would progress causing illness and death if not promptly and adequately treated. As the years passed the fact became apparent that all reactors to tuberculin have lesions of the primary type determinable as to location in only a small percentage during life. Observation of such children under different conditions showed that whether they received sanitarium care or remained at home there was no difference in the morbidity or mortality when the cases were reviewed some years later. [Actually the prime necessity for hospitalizing those with primary tuberculosis is to remove them as a focus of infection or to give them the advantage of a better environment and better nutrition with which to cope with this disease.]

In the course of many surveys so-called benign shadows are often seen and Dr Myers feels that serious injustice could result from a recommendation of treatment for every lesion found on the first examination as many of them regardless of size have long since been controlled by the body defense mechanism and therefore require no treatment. Unfortunately the status usually cannot be determined except by extended observation, and as age advances there is an accrual of minimal lesions that have come under control. These lesions are early.

In conclusion Dr Myers says that inexpensive x ray inspection of the chest of each adult would reveal practically everyone who at the time has infectious tuberculosis. Those who react to tuberculin on the first test and those who are later found to be reactors should have a thorough annual examination and be

ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Experiences in Ventriculography of Tumours Below the Tentorium Erik Lysholm *Brit J Radiol* 19 437-452 November 1946

This study of subtentorial tumors is based on cases seen in Olivecrona's Neurosurgical Clinic in the Serafimer Hospital, Stockholm. The greater part of the paper consists of illustrated case reports. Unfortunately the reduction required by printing makes the cuts difficult to interpret, at least to the eye of the abstractor.

Since 1935, 8 verified lesions of the quadrigeminal plate had been seen. Exact localization was made roentgenographically in 3 cases. In 2 cases an expanding process behind the aqueduct bulging into the posterior part of the third ventricle was identified. In 3 cases only obstruction to the aqueduct could be seen.

Ventriculography was done in 58 cases of vermian tumors, all verified. In 49 of these there was accurate localization, in 5 the localization was slightly inaccurate and in 4 only an infratentorial tumor was identifiable.

Of 75 cases of hemisphere tumors there was exact localization in 71, a vermian lesion was diagnosed in 2 and non specific infratentorial localization in 2.

All but one of 11 tumors of the pons were accurately localized.

There were 33 cerebellopontine angle tumors, all accurately localized. 21 of these were acoustic tumors. This represents about 10 per cent of the acoustic tumors. The other 90 per cent had bony changes and ventriculography was not required.

Of 93 cases of infrafalx tumors 88 were exactly located. Forty-two ventriculograms were negative where an expanding process was suspected in the posterior fossa. In only 5 of these cases was operation done, revealing 2 meningiomas, 1 brain stem tumor, 1 acoustic tumor and 1 tumor of the fourth ventricle.

SYDNEY J. HAWLEY, M.D.

Cystic Teratomas and Teratoid Tumors of the Central Nervous System in Infancy and Childhood Franc D. Ingraham and Orville T. Bailey *J Neurosurg* 3 511-532 November 1946

Fifteen cases of cystic teratoma and teratoid tumor of the central nervous system in children found among 231 neoplasms of the central nervous system operated upon at the Children's Hospital, Boston in a twenty year period are reported. No patients over fifteen years of age are admitted to this hospital. Eight of the tumors were intracranial and 7 intraspinal. Cranio-pharyngiomas and sacrococcygeal teratomas have been excluded from this series as have chordomas. Dermoid cysts however are included.

Intracranial Group From the clinical point of view the character of the symptoms and the problems of differential diagnosis of intracranial teratomas and teratoid tumors were those of any space-occupying lesion in that location. There were local effects depending on the site of the tumor and pressure effects resulting from the increase in volume of the cranial contents. Nothing was encountered that would suggest the pathological diagnosis preoperatively unless an associated congenital anomaly was present which occurred

occasionally. The presence of a congenital anomaly in a patient with signs and symptoms of a space-occupying cerebral lesion does not establish the diagnosis of teratoma or teratoid tumor but increases somewhat the chances of finding this lesion. Roentgenograms of the skull may possibly show calcified areas suggesting the presence of bone or other organoid structures in tumors of this group. In none of the patients in this series was it possible to make a definite diagnosis of the type of lesion roentgenologically. There was evidence of increased intracranial pressure and in some instances internal hydrocephalus was present. Ventriculograms or encephalograms demonstrated filling defects indicating the size and location of the tumors. Of the 8 patients with intracranial teratoma or teratoid tumor 1 is living more than five years after operation, 2 are living for periods less than five years, and 5 are dead.

Intraspinal Group As with the intracranial teratomas and teratoid tumors the symptoms produced by the intraspinal members of the series were those of a space occupying lesion at the level involved. With the intraspinal tumors however the association of a congenital abnormality was the rule rather than the exception. Since these anomalies affected the vertebrae, they could be easily demonstrated roentgenologically and often by physical examination as well. The bony defects might or might not occur at the same level as the tumor. They were of considerable importance in suggesting the diagnosis of teratoma or teratoid tumor preoperatively. Usually the anomalies were compatible with normal function of the spine once the tumor had been removed and seldom required operative treatment. Occasionally also nevi or pigmented spots in the skin at the level of the lesion were regarded as somewhat suggestive of teratoma or teratoid tumor. Congenital anomalies of other organ systems such as the cardiac or genito-urinary system are not regarded as being in any way related to the incidence of intraspinal tumors.

Roentgenograms were chiefly useful in this group of patients' or the demonstration of anomalies of the vertebral column. It is conceivable that a definite diagnosis might be made roentgenologically by the demonstration of calcified organ like portions of the tumor. As in the intracranial group no such instance occurred in the present series. Other roentgen studies for further localization and definition of the extent of the growth were made as indicated as with any intraspinal tumor. Of the 7 patients with intraspinal teratomas and teratoid tumors 2 are living more than five years, 4 are living for periods less than five years, 1 is dead.

THE CHEST

Transverse Laminagraphy of the Chest Pietro Amisano *Radiol med (Milan)* 32 418-421 November 1946

The author has applied laminagraphy to the study of transverse sections of the chest. The patient is in a sitting position with the head flexed on the chest and the film is under the thighs. The axis of rotation of the laminagraph is at the level of the chest to be examined. The roentgen rays enter the body at the shoulder level and traverse the whole trunk before reaching the film.

sion and repeated at three-month intervals. In children "negative" roentgen findings were not taken as final, and in a number of instances the primary lung infiltration, which was not visible in the first roentgenogram, became apparent in later films. The type of lesion varied according to age. The primary complex was found in most of the children and hematogenous foci were the rule in adults. The respiratory tract thus appears to be the route of entry even in tuberculosis of the bones and joints. The skeletal lesion in most children originates soon after the primary infection. In adults it is usually due to reactivation of quiescent tuberculous foci resulting in blood stream dissemination and subsequent implantation in bone and lung.

The importance of routine roentgenography of the chest in the diagnosis and prognosis of skeletal tuberculosis is emphasized.

Extrapleural Pneumothorax in Silico-Tuberculosis
H M Maier and A Hurst. *Am Rev Tuberc* 54: 509-511, December 1946

A case of silico-tuberculosis is reported in which extrapleural pneumothorax was instituted and resulted in prompt closure of a tuberculous cavity. The method is recommended for trial in cases of this type since it is a reversible procedure and since other methods of collapse therapy often cannot be employed in silico tuberculosis.

L W PAUL M D

Pneumatocele During the Course of Pneumonia in Children
John Roger Almklöv and Alexander Hatoff. *Am J Dis Child* 72: 521-528 November 1946

A cavity with a sharply defined thin border and often an air fluid level is a fairly frequent roentgenologic finding during the course of pneumonia in children. To designate this the authors prefer the term 'pneumatocele' to emphysematous bulla or benign cavity.

Normally the bronchial tree dilates in inspiration and is constricted in expiration. When inflammatory swelling of the bronchial mucosa accompanies pneumonia it may lead to a check-valve action allowing more air to enter during inspiration than can pass out in expiration and an obstructive emphysema results.

The diagnosis of pneumatocele is usually made on roentgen study. Conditions to be differentiated are acute pulmonary abscess, putrid pulmonary necrosis due to infarction, tuberculous cavity, loculated pneumothorax and congenital pulmonary cyst (Caffey. *Am J Dis Child* 60: 586 1940). Acute pulmonary abscess develops and heals slowly and is accompanied by foul sputum, fever, clubbed fingers and other signs completely absent in pneumatocele. Tuberculous cavities are ruled out by negative reaction to tuberculin and uneventful course. Loculated pneumothorax may be excluded by lateral and oblique chest films. Congenital pulmonary cysts are demonstrable before, during and after the course of pneumonia, whereas pneumatocele is not usually present on the first films and disappears during the course of the disease.

Pneumatocele rarely produces symptoms or signs and in uncomplicated cases requires no treatment.

The authors saw 7 cases of pneumatocele in 50 children with pneumonia in a one year period. Five of the patients had lobar pneumonia and 2 bronchopneumonia with localization in the middle portion of the right lung field. The pneumatocele invariably occurred in the area involved by the pneumonia. The time of appearance varied from the second to the twenty fifth

day after onset of the disease. In 3 of the 7 cases more than one pneumatocele developed. The lesions varied from 1 to 3 cm in diameter. Fluid levels were seen in 5. The pneumatoceles were observed from four to forty-one days from date of appearance to disappearance. All disappeared spontaneously and completely without special treatment of any kind directed to the pneumatoceles.

BERNARD S KALAYJIAN M D

Bronchial Adenomas
Sion W Holley. *Mil Surgeon* 99: 528-554 November 1947

Bronchial adenomas constitute approximately 8 to 10 per cent of all primary bronchopulmonary neoplasms. They usually occur in the third and fourth decades, hence they have been encountered with relative frequency in the larger Army hospitals. The favorable outcome to be anticipated in these cases is in decided contrast to the grave prognosis in bronchiogenic carcinoma, but early diagnosis is essential for proper treatment. This study is based upon records and specimens from 39 cases at the Army Institute of Pathology. Seven cases from this number are presented to illustrate various clinical and pathologic features of the tumor.

Fourteen of the patients were female, 25 were male. The neoplasm was discovered during life in all but one instance in which a 6-mm nodule of the carcinoid type was found after death from hypertensive heart disease. Cough was a symptom in 66 per cent of cases, hemoptysis (including blood-streaking as well as severe hemorrhage) in 44 per cent, expectoration in 40 per cent, some form of chest pain usually mild in 36 per cent, fever in 36 per cent, dyspnea in 20 per cent, weight loss in 11 per cent, and wheeze in 9 per cent. Thirty-three per cent of the patients had had one or more attacks of acute pulmonary infection, apparently secondary to bronchial obstruction. Roentgenographically the tumor was demonstrable in 8 cases: atelectasis in 16, and inflammatory infiltration in 9 others. The affected bronchus was partially or completely obstructed in 19 cases. Bronchoscopic biopsy was performed in 34 cases, resulting in immediate diagnosis of adenoma in 18, the same diagnosis after additional biopsy or review of the original sections in 5, carcinoma in 14, cylindroma in 1, and endobronchial sarcoma in 1.

The tumor was removed bronchoscopically in 9 cases. There were 11 lobectomies with two lobes of the right lung removed in two instances. Pneumonectomy was performed in 15 cases.

Three of the 38 patients in whom the tumor was diagnosed during life have since died. At the last follow-up examinations of the remaining patients there was local recurrence in one, hepatic metastases were found at laparotomy in another. In one patient with a mixed tumor type of bronchial adenoma, no further attempt at removal was made after the original bronchoscopy. This patient had had partial collapse of the right lung and bloody pleural effusion for three years. The last roentgenogram showed rounded pleural densities which might be interpreted as tumor nodules. The longest period of observation after operation was ten years. Nothing is known of 3 patients after the immediate postoperative period.

The tumors were located at or near the pulmonary hilus were usually polypoid and in several instances attained rather large size. They assumed two distinct patterns, one which simulated that of appendiceal carcinoid and the other that of some of the mixed tumors of

isolated in hospitals and sanatoria if the disease becomes infectious. The responsibility for these accomplishments lies with those in charge of the public health. Failure to achieve them—failure to control completely and ultimately to eliminate tuberculosis—is unpardonable.

[No mention is made of the case which is first seen as a minimal case but may have in the past been a moderately advanced or advanced case. These are the cases of minimal disease which are much more likely to break down than are lesions which were actual minimal to begin with. In this way, the x ray shadows may be misleading, and when minimal arrested lesions are seen one must keep in mind the possibility of a formerly existing more advanced lesion.—S F T.]

SYDNEY F. THOMAS, M.D.

Tuberculosis—A Labor Problem. Leo Price. *Am Rev Tuberc* 54 512-526 December 1946

The author discusses some of the social and economic problems of tuberculosis as it affects the average worker. The laboring man often shuns tuberculosis case finding programs because he knows the discovery of the disease in himself means the loss of a job, hospitalization, impoverished dependents, and trouble in finding work after the disease is stabilized. The experience of the Ladies Garment Workers Union in establishing a tuberculosis insurance program is discussed in considerable detail. This union, which now numbers 165,000 members in New York City, began such a program in 1913. In 1942 union contracts first contained a clause requiring the employers to pay a tax on the pay roll for health aids to employees. With these funds improved medical service for garment workers became possible. Members of the union co-operate with x ray surveys for the detection of tuberculosis because of the assurance that the victims of the disease will receive medical and economic support. A long range tuberculosis control program sponsored by industry should consist of periodic x ray examinations, sanatorium care and financial aid for tuberculous patients, rehabilitation in sheltered workshops and medical supervision of all workers who have ever had the disease. L. W. PAUL, M.D.

Cancer and Pulmonary Tuberculosis. Diagnostic Problems in Patients with Cancer of the Lung in the Presence of Pulmonary Tuberculosis. Bruno Gerstl, Frederick C. Waring, Jr., and Kirby S. Howlett, Jr. *Am Rev Tuberc* 54 470-487 December 1946

Since January 1940 7 cases of coexisting bronchiogenic carcinoma and pulmonary tuberculosis have been recognized at Laurel Heights Sanatorium, Connecticut, among approximately 1,600 patients sent in with a diagnosis of pulmonary tuberculosis only. The present report summarizes the findings in these cases.

In only one instance did the diagnosis of tuberculosis present a problem in the remaining cases the diagnosis was readily apparent and was promptly confirmed by the finding of tubercle bacilli in the sputum. The detection of the cancer was more difficult. The clinical evidences of cancer tended to be masked by the symptoms and signs of tuberculosis. The x ray findings were of greatest significance in at least causing a suspicion as to the presence of another disease. When true hilar infiltration is demonstrated on postero-anterior and lateral films cancer should be suspected since this is seldom seen in reinfection tuberculosis. Evidence of

major bronchial obstruction or of a relatively circumscribed mass should also arouse a suspicion of the co-existence of carcinoma, especially in older patients. When such suspicion is aroused the well known diagnostic procedures available for confirmation of carcinoma should be employed including bronchoscopy, biopsy of suspected metastatic lesions, needle biopsy, etc.

None of the cases reported was deemed operable at the time of diagnosis but since pulmonary resection is now feasible in many cases of tuberculosis the practical desirability of earlier diagnosis of coexisting cancer is apparent.

L. W. PAUL, M.D.

Mass Miniature Radiography. A Survey in the United States Army Air Forces. Edgar Wayburn. *Am Rev Tuberc* 54 527-540 December 1946

During 1945 a mass x ray survey of the chest was conducted on 77,480 persons in the United States Army Air Forces in England by means of two mobile trailer units. The results of the survey are presented in a series of tables and charts. In this select group there was found 0.006 per cent of active primary tuberculosis, 0.08 per cent of active reinfection type tuberculosis, and 0.26 per cent of healed reinfection type tuberculosis. Chest conditions of clinical interest other than tuberculosis were found in 78 cases. There was nothing in the survey to suggest that flying predisposes to pulmonary tuberculosis in previously healthy young men.

L. W. PAUL, M.D.

Endogenous versus Exogenous Origin of Reinfection Type Pulmonary Tuberculosis. With Case Report. William H. Harris, Jr. *U S Nav M Bull* 46 1702-1707 November 1946

'Reinfection tuberculosis' is a term applied to that form of the disease which occurs after a primary lesion has been sustained. It has also been termed 'adult type tuberculosis', 'secondary infection', and 'super infection'. As applied to reinfection tuberculosis, endogenous origin indicates that the bacilli causing the disease process have been derived from an old primary infection and exogenous origin implies that the causative organisms have come from an outside source. The exogenous route is generally considered to be of greater frequency and of greater importance.

A case of reinfection pulmonary tuberculosis is reported here with x ray evidence and lack of outside contacts strongly suggesting an endogenous origin. Roentgenograms are reproduced which indicate a breaking down of an old calcific hilar lesion permitting a spilling of viable bacilli which were believed to be responsible for the reinfection. The role of atypical pneumonia in the excitation of latent primary lesions with resultant endogenous reinfection is emphasized.

Lung Lesions in Skeletal Tuberculosis. Review of 500 Cases. K. J. Mann. *Lancet* 2 744-749 Nov 23 1946

In an investigation of the respiratory tract in 500 patients with skeletal tuberculosis, 284 cases (57 per cent) of active pulmonary tuberculosis were found. The history, symptoms, signs, and bacteriologic studies were of little assistance in discovering early lung involvement and it was necessary therefore to rely on roentgen examination for diagnosis and classification of pulmonary lesions. Roentgenograms were taken on admis-

border is usually hidden by the vertebral column and hence an erroneous diagnosis of cardiac enlargement may be made. The right hilar shadows, normally obscured by the overlying right cardiac border, may appear unusually prominent. From these findings a presumptive diagnosis of funnel chest can be made in the absence of other lesions which might cause a left cardiac shift such as scoliosis, left pleural thickening, left-sided atelectasis, right-sided pleural fluid, and tumors. The lateral view confirms the presence of the deformity.

Several instances of electrocardiographic abnormality occurring in association with funnel chest have been reported. Right axis deviation is a frequent finding, left axis deviation is less common. All varieties of T-wave change, including voltage elevation, peaking and diphasic and negative complexes have been reported. ST elevation of minimal degree has been noted. The PR interval is usually unchanged. The changes occurring in the chest leads have not previously been reported. The authors found T wave changes in lead CF-4 to be the most constant variation in their series.

Disturbances of rhythm occurring in association with funnel chest are uncommon. One of the authors' patients presented a bigeminal rhythm due to regularly recurring right ventricular extrasystoles. This was attributed to an irritable focus in the right ventricle resulting from the constant pressure of the deformed sternum in this region.

Symptoms of a serious nature are uncommon. Palpitation and dyspnea on exertion are the most common complaints. Chest pain occurred in 4 of the cases but was not of the type usually associated with organic heart disease. Significant cardiac physical findings were present in only one case. The blood pressure was within normal limits with the exception of a slight systolic elevation in one patient. Slight cyanosis of the nail beds was observed in two cases.

Surgical treatment is indicated only in a few cases in which there are clear-cut findings of increased cardiac embarrassment not attributable to other conditions.

H. H. WRIGHT, M.D.

Heart Disease in the Case-Finding Program

Howard F. West. *Am Rev Tuberc* 54: 465-469, December 1946.

In the interpretation of films made during mass surveys of the chest, alteration in the size and shape of the heart and great vessels may be detected and should be reported. When miniature films are employed, accurate measurements of size may be difficult to make, but methods have been suggested which may be useful in borderline cases. In a recent survey made by the Heart Division of the Los Angeles Tuberculosis and Health Association of 8933 industrial workers the 4 X 5-inch films were interpreted as suspicious for heart disease in 151 instances. At the time of analysis, 116 of these persons had been studied clinically and in approximately 75 per cent clinical confirmation of heart disease was obtained.

Since a considerable portion of cases of unsuspected heart disease can be recognized by essentially the same technique used in finding early tuberculosis it is important to decide what use can and should be made of this information. It is suggested that the National Tuberculosis Association and the American Heart Association establish a joint committee to consider the problem of joint case finding in its entirety. Standards

of procedure, technical, clinical and social can be adopted for the guidance of local groups in the field.

L. W. PAUL, M.D.

Study of Blood Currents Within the Heart. Adamo Grilli. *Radiologia (Rome)* 2: 249-292, 1945.

The author has had the opportunity of observing 2 cases of free intraventricular bullets in which the movement of these foreign bodies gave a good indication of the action of the blood during a normal cardiac cycle. These patients were studied fluoroscopically and with kymographs obtained by means of fixed and moving grids and the existence of whirlpools and eddy currents was clearly demonstrated.

CESARE GIANTURCO, M.D.

THE DIGESTIVE SYSTEM

Roentgenologic Examination in Patients with Bleeding from the Gastrointestinal Tract. Richard Schatzki. *New England J Med* 235: 783-786, Nov 28 1946.

The routine procedures in examination of patients with gastro-intestinal hemorrhage will vary with the patient and the history at the time of bleeding. Very often the best procedure is a scout film of the abdomen followed by examination of the large bowel. Since massive hemorrhages are in the majority of cases from the upper gastro-intestinal tract, it is often advisable to examine only this portion.

In recent years examination of the upper gastrointestinal tract at an early date after bleeding occurs has been an accepted procedure. It may be done within twenty-four to forty-eight hours of the initial bleeding or shortly thereafter. Shock is of course a contraindication to examination, but this is not true of active bleeding in itself since there is no reason to believe that the watery suspension of barium sulfate is as dangerous as food.

The patient should be first placed on his back rotated slightly to the left. A single swallow of barium, if followed fluoroscopically through the esophagus may reveal the presence of varices. Two or three additional swallows will outline the posterior part of the gastric fundus. With rotation to the right, the antrum and possibly the duodenal bulb will be observed after which the patient may again be rotated to the left, in which position the barium-coated gastric wall will be outlined with air displaced from the fundus. Examination of the esophagus in both oblique diameters is completed with the patient prone. The duodenal bulb is examined in the same manner. Very often the cause of the bleeding will be found in this part of the examination, in which case further study is unnecessary. Palpation is omitted and the peristaltic activity with rotation of the patient is utilized to bring out any significant lesion. Additional barium may be needed to fill the stomach completely and give adequate definition to the distal portion. Occasionally ulcers in the fundus may be seen best in the right oblique view, while those of the antrum and the duodenal bulb may be best seen in the left oblique projection. The patient may then be turned in the prone position where the lesser curvature and duodenal bulb are more adequately defined. The second and third portions of the duodenum should be carefully observed and if no source of bleeding is discovered the meal should be followed through the small bowel at appropriate periods.

salivary glands and other structures of the mouth and face. The origin of neither of the types was determined, though their intramural location in the bronchus suggests bronchial glands or ducts as sources. Several of the tumors showed features of malignancy, some had infiltrated locally.

This study indicates that lobectomy or pneumonectomy according to the location of the tumor, is the preferred treatment (1) because many of the tumors are of such size or have infiltrated so that they cannot be entirely removed through the bronchoscope, (2) because of the malignant potentialities of some of the tumors, and (3) because of the frequent coexistence of bronchiectasis and chronic pneumonitis.

Broncholithiasis John H. Barrett Arch Otolaryng 44 574-580, November 1946

A case of broncholithiasis is recorded. The patient's illness began with influenza in December 1943. This was followed by a persistent cough and then pneumonia in October 1944, which was treated with penicillin, with relief of all symptoms but the cough. In February 1945 the fever recurred and the cough became severe. A month later a sharp pain in the chest developed, and the patient had a severe paroxysm of coughing and raised a large amount of bright blood. Roentgen examination revealed consolidation of the middle lobe of the right lung, with some irregular diminished aeration in the anterior portion of the lower lobe. The right diaphragm was elevated. The heart was displaced slightly to the right but was otherwise normal. There was a dense calcification measuring 1 by 1.4 cm in diameter just to the right of the mid line in the region of the right main stem of the bronchus. The changes in the middle lobe of the right lung, with cardiac displacement suggested an atelectatic process with infection. On bronchoscopy, a calcareous mass surrounded by granulation tissue was found to obstruct the lumen of the right main bronchus just above the orifice of the middle lobe. This was removed and proved to be a grayish white rough, irregular calculus about 1 cm in diameter. On further questioning the patient recalled coughing up a similar but smaller calcified mass which however had not been shown to the attending physician.

Primary Endothelioma of the Pleura. Herman Weissman Dis of Chest 12 562-570, November-December 1946

Primary endothelioma of the pleura is a rare neoplasm, and its early diagnosis saves the patient a great deal of ineffectual therapy. The onset is gradual and usually becomes apparent following a respiratory infection. Pain appears early and is intermittent in the beginning gradually becoming constant and gnawing. Usually it is not affected by respiration or cough and is not relieved by fluid formation or aspiration. An idiopathic pleural effusion after middle age may be the first clinical manifestation. Dyspnea and a dry irritating cough progress as the disease advances. The physical findings are those of a pleural effusion. On aspiration, the needle encounters great resistance as it passes through the pleura. Other signs may appear as clubbing of the fingers, unilateral or bilateral vocal paralysis, dilatation of the thoracic veins etc. The course is brief with progressive cachexia, weakness, increasing dyspnea, cyanosis, coma and death.

The x-ray findings are helpful but not in the early stages. After thoracentesis, a pneumothorax should be induced. The characteristic findings are multiple smooth tumor nodules of varying sizes and thickness, mostly over the parietal pleura.

The author gives historical and statistical data, quotes Ewing and others as to the origin of the tumor and presents two case histories, in one the diagnosis was verified postmortem, and in the second by a biopsy.

HENRY K. TAYLOR, M.D.

Mediastinal Alterations Secondary to Hypertrophy of the Left Auricle. Stratigraphic Study. Pietro Perona and Franco Hueber Radiol med (Milan) 32 440-448, November 1946

The authors have studied the angles formed by the two main bronchi with the trachea in normal sthenic and hyposthenic individuals. The average angles found for sthenic types are between 35° and 42° for the right bronchus 39° and 43° for the left bronchus. The average angles for hyposthenic types are 30° to 33° for the right bronchus and 34° to 36° for the left bronchus.

In patients with hypertrophy of the left auricle, the authors found a widening of the angle between the trachea and the bronchi as well as some compression of the bronchi, with reduction of their volume.

CESARE GIANTURCO, M.D.

Radiological Visibility of the Normal Thymus. Enrico Benassi Radiol med (Milan) 32 413-417, November 1946

According to MacNeil Hardy, Little and Blaklan, a large upper mediastinal shadow will be found in 50 per cent of the infants examined by roentgen rays. The author has found large upper mediastinal shadows in many infants referred because of other complaints and ascertained that the widening of the mediastinum was due to the thymus since the width decreased following irradiation. The author believes that the size of the normal thymus varies between wide limits, and that roentgen therapy should be used only in those cases in which there are definite symptoms of obstruction.

CESARE GIANTURCO, M.D.

Roentgen and Cardiac Manifestations of Funnel Chest. J. George Teplick and E. H. Drake Am J Roentgenol 56 721-735, December 1946

Funnel chest is not a rare condition but since most persons having this deformity are without troublesome symptoms only a small number of cases have been reported. The authors present 9 cases and discuss the salient clinical roentgenographic and electrocardiographic features.

The malformation is a developmental anomaly in most instances and is often noted in more than one member of the same family. Severe rickets may produce the deformity, although pigeon chest is a more common result of that disease. Severe trauma to the sternum with an angulated fracture is also an etiologic factor. The condition is due to posterior displacement of the sternum, the manubrium not usually being involved. The depression of the body of the sternum may amount to 7 cm or more. The heart is usually shifted toward the left and cardiac rotation in the sagittal plane may be present. The left border of the heart shows some elevation from the diaphragm resembling a right ventricular enlargement. The right cardiac

ated with changes in the bulb that simulate the changes seen in peptic ulcer. One of the disturbing features of the lesion is the rapidity with which a partially filled duodenal cap spills into the descending loop of the redundancy. This should not be confused with irritability or deformity with failure of filling. In the erect position, flattening or peaking at the cap may occur because of the traction of the mobile U shaped loop. At the angle formed by the bulb and the descending limb of the redundancy, the mucosal folds overlap and interlace. A stellate mucosal pattern at this point may be analogous to the stellate formation often seen at the superior angle of the normal duodenum. In the case of the redundant duodenum, this shadow may occur close to the pylorus and is likely to be interpreted as a crater or scar. A large flaccid bulb often has much the appearance of a redundancy of the superior duodenum but careful observation of the progress of the barium should settle this problem.

In each case careful scrutiny of the bulb itself must be made so that the apparent deformity and irritability associated with redundancy of the superior duodenum will not be confused with intrinsic duodenal disease.

In the entire series of 1,000 gastro intestinal examinations, there were 248 instances of definite disease in the stomach or duodenum. This includes ulcers and cancers but not gastritis or duodenitis. Six of the 22 patients with elongation of the superior duodenum showed a defect in the stomach or duodenum. Since the figures in each group approximate 25 per cent the authors believe that the redundant duodenum is not a contributing factor to either gastro-intestinal pathology or symptomatology."

Amebic Disease of the Cecum. Clinical and Radiological Aspects. Dwight L. Wilbur and John D. Camp. *Gastroenterology* 7: 535-548, November 1946.

Amebiasis frequently involves the cecum and presents a variety of clinical pictures simulating a variety of cecal and appendiceal lesions. Symptoms may be absent. Some of the patients in the authors' series with amebiasis had had a previous diagnosis of acute appendicitis, appendiceal abscess, and carcinoma of the cecum. The frequency with which the diagnosis of acute appendicitis is made in these cases is of great importance because of the disastrous results of surgery (the mortality following surgical therapy incident to the Chicago epidemic of 1933 was 40 per cent).

In the authors' experience roentgen examination of the colon was the most valuable method of indicating the presence of amebic disease. In numerous instances the diagnosis was suspected or made by the roentgenologist when there were no clinical symptoms in cases with or without cysts or trophozoites in the stool. The significant roentgenologic changes in the cecum consist of spasm, dilatation, relaxation and abnormal patency of the ileocecal valve, inflammatory induration with edema, and inflammatory tumefactive defects. The earliest lesions are those involving the mucosa, the cecal walls lose their sharp smooth character and the mucosa appears finely granular or of irregular contour and there may be associated cecal spasm. Cecal lesions of amebiasis were found by barium enema studies in 9 of 37 patients with stools which on routine examination contained cysts or trophozoites of *Amoeba histolytica*. Roentgen examination was particularly useful in indicating the diagnosis of amebiasis in patients with a history suggesting previous disease of the appendix and

in those with hepatitis otherwise unexplained, enlarged livers, and abscesses of the liver, when no amebae or cysts could be found in the stools or pus.

With the return of military personnel from heavily infested areas, a considerable number of cases of amebiasis will be observed in the United States, and clinicians and roentgenologists should be on the alert for signs of this disease.

A Concept of Paralytic Ileus. A Clinical Study. John Devine. *Brit J Surg* 34: 158-179, October 1946.

Paralytic ileus is of three types: (1) idiopathic paralytic ileus, (2) paralytic ileus arising from medical diseases, (3) paralytic ileus the result of surgical operations. A number of brief case histories are given illustrating these three types. The pathological physiology is reviewed and the author quotes Wangenstein (1942), who showed that a pressure of 55-65 mm. Hg within the gut causes pressure on the veins encircling the ileum. This interferes with the absorption of gas and fluid and leads to more distention. The effects of distention may be local or general. One local result is increased permeability of the capillaries of the intestinal mucosa with transudation of some of their contents into the peritoneal cavity. There is a resulting loss of plasma from the circulation with decrease of bowel motility probably from associated edema of bowel. Among the general effects is diminished flow of bile. In most of the cases studied by the author there was little or no sign of bile in the aspirated fluid. In a fully developed paralytic ileus the large intestine is also involved and enemas are retained or returned without result.

In a lengthy discussion of various treatments of paralytic ileus the author enumerates those drugs and procedures which are used to increase motility, and reviews the literature on the action of morphine on the small intestine—a drug frequently used not only for its action on the muscle of the small intestine, but also for the induction of sleep and relief of pain. In 3 cases tracings and observations were made on patients with the Miller-Abbott tube and recording tambour. The results of these and other investigations seem to show that morphine: (1) delays the passage of food through the intestine and therefore causes constipation, (2) causes duodenal spasm for a short time followed by relaxation, (3) decreases peristaltic movement of the duodenum and ileum but (a) increases the tone and (b) the frequency of the small mixing waves. Cases treated with the harbiturates were also studied by means of a recording Miller-Abbott tube and it is concluded that they should be given with caution in cases of possible paralytic ileus as they decrease peristalsis and tone.

Coincident pathological conditions which may contribute to the occurrence of postoperative paralytic ileus are hypoproteinemia, distention of the upper urinary tract or bladder, intraperitoneal irritation, and over-distention of the stomach.

The author develops a concept of ileus based on clinical study employing auscultation of the abdomen and the Miller-Abbott tube with recording tambour. According to this concept there are three stages of ileus: (1) the stage of no movement, (2) a stage of disordered and inco-ordinated movement, (3) a stage when movement is being co-ordinated once more. Stimulation by enemas, pituitrin or by other measures in the second stage causes more distention and increased pain and discomfort for the patient. In the third stage

When the source of bleeding has not been found, re-examination at a later date, when palpation is possible, should be made. In spite of all the maneuvers that roentgenologists may practise, the source of bleeding may not be discovered.

The most frequent cause of bleeding is duodenal ulcer, and careful examination of the duodenal bulb is imperative. Gastric ulcers may also cause bleeding and, if they are small may disappear within a two week period. Cancer of the stomach may be the source of bleeding but a large blood clot may simulate a polypoid tumor. Re-examination would exclude this possibility. The bleeding may be from varices of the esophagus and these are sometimes hard to demonstrate. They may be present even in the absence of splenomegaly, ascites and a palpable liver. The varices may be demonstrated only after the bolus of barium has passed through the esophagus and while it is outlined by a thin coating. The diagnosis of gastritis as a source of bleeding is difficult, and is possible in only a small number of cases. Hemorrhage may result from a hiatus hernia. Repeated hemorrhages may occur in the presence of submucosal tumors such as leiomyoma, fibroma and neurofibroma of the stomach.

Lesions of the small bowel and colon are not considered in this discussion. JOHN B. McANENY, M.D.

Gastrocolic Fistula. A Clinical and Experimental Study. R. John F. Renshaw, Frederic E. Templeton, and Robert M. Kiskaddon. *Gastroenterology* 7: 511-521. November 1946.

Gastrocolic fistula is one of the most serious complications of surgical treatment for peptic ulcer. The fistula produces a devastating syndrome characterized chiefly by diarrhea, steatorrhea, weight loss, anemia, and malnutrition. Because of the conflicting opinions about the physiological cause of the syndrome and because the shunt mechanism or by passing of the small intestine did not seem to afford an adequate explanation, the authors made gastrocolic, gastroyejunocolic and enterocolic anastomoses in dogs, observed the results and compared them with observations in human patients having similar fistulas.

Between 1921 and 1946 20 patients with proved gastrocolic fistulas were seen at the Cleveland Clinic. Ten of the 20 patients had roentgen studies with sufficient evidence for analysis of direction of the flow of barium. Eight of these 10 patients had fistulas following operation for peptic ulcer. The roentgen studies revealed that the barium meal passed from the stomach into the upper small intestine. In 2 of the 10 patients, a small or minor portion of the meal passed through the fistula into the colon while the major portion passed from the stomach into the upper small intestine. In the other 8 patients the entire meal passed from stomach to small intestine and none went directly from stomach to colon. It is significant that all or the larger part of the meal always passed into the upper small intestine and was never shunted or dumped directly into the colon.

Seven dogs with gastrocolic or enterocolic anastomoses 1 to 4 cm. in diameter had diarrhea, steatorrhea, anemia and malnutrition similar to the syndrome occurring in human beings with gastrocolic or gastroyejunocolic fistulas. In all the animals roentgenologic studies revealed that all or the major part of the barium meal passed from the stomach into the upper small intestine. In one dog the barium meal was ob-

served to pass from stomach into small intestine, then into the colon, and finally regurgitate through the fistula back into the stomach from which it then passed into the upper small intestine again. In another dog fecal material flowing from the colon into the stomach through the fistula was observed at gastroscopic examination.

In one human patient with gastroyejunocolic fistula the barium meal was observed to pass through the pylorus and fistula. Twenty-four hours later most of the barium was still scattered through the small intestine and colon. The stomach contained more barium at twenty-four hours than at five hours, indicating regurgitation through the fistula back into the stomach.

Five dogs which were killed during the course of the syndrome or died as a result of the syndrome showed pathologic changes in the stomach of an inflammatory nature. Two dogs showed gastric ulceration with evidence of organization and some degree of chronicity. In the small intestine, especially the upper third there was a striking subacute to chronic type of inflammatory infiltration limited almost exclusively to the mucosa of the papillae.

Tentative conclusions based on the above evidence and observations of others are: (1) Sufficient aliment passes from stomach into upper small intestine to maintain adequate nutrition. (2) Passage of aliment directly from stomach to colon is not frequent enough nor in large enough amounts to produce the syndrome. (3) Deranged digestive and absorptive functions of the small intestine cause the syndrome. (4) Derangement of small intestinal function is probably the result of damage to the intestinal mucosa by passage of colonic contents through the small intestine.

Redundant Duodenum. A Radiographic Study. Irvin H. Slater and Arthur Lautkin. *U. S. Nav. M. Bull.* 46: 1651-1657, November 1946.

The superior portion of the duodenum is usually a short segment which proceeds posteriorly and to the right to form the first part of the normal horseshoe-shaped duodenum. Occasionally there is elongation of this segment, producing a U or V shaped redundancy demonstrable on roentgen examination. In a series of 1,000 consecutive gastro-intestinal examinations at a naval hospital 22 cases (2.2 per cent) of redundant duodenum were found. In most of the cases in this series the segment was mobile.

The V shaped tract shows no dilatation and usually has an entirely normal mucosal pattern. The U shaped loop however is dilated and as a rule, presents a water trap appearance. This segment often seems to retain the barium for a short interval in its relatively wide channel, giving an appearance of "puddling" which is transient and not to be confused with retention. In no case in the series reported here was prolonged retention or even significant delay in the emptying of this segment observed. The barium meal passed normally through the duodenum and in no instance was an empty stomach associated with anything but an empty superior duodenum.

Chronic duodenal obstruction may however be associated with dilatation and elongation of the superior duodenum. In these cases a U shaped redundancy has been noted. This should be differentiated by its obstructive concomitants—gastric retention and failure of normal progress of the meal into the jejunum.

Elongation of the superior duodenum may be associ-

The appearance of monostotic fibrous dysplasia in the roentgenogram offers little that is characteristic. In the long bones the lesions were found principally in the metaphyses though occasionally they occupied the middle of the shaft. No site of predilection was noted in the ribs. When the skull was affected, the maxilla was most often involved. In the roentgenogram, the area of fibrous dysplasia is radiolucent, sometimes traversed by delicate trabeculae of bone. It is usually central in position and produces thinning and expansion of the cortex, particularly marked in the ribs and fibula and in the bones of the calvarium. At times there is a narrow margin of condensed bone at the periphery. The non-specificity of the roentgenographic appearance in this disease is emphasized by the fact that in not one of these cases was the possibility of fibrous dysplasia entertained by the roentgenologist. The diagnoses offered in order of their frequency were bone cyst 16, giant-cell tumor 8, osteochondroma 3, tumor 7, enchondroma 4, chondroma 3, fibroma, ossifying fibroma, osteitis fibrosa cystica, sarcoma and myeloma 2 each. Osteoma, chondromyxoma, non-osteogenic fibroma, adamantinoma, Ewing's tumor, eosinophilic granuloma of bone, Paget's disease, osteomyelitis, and callus each appeared once.

The pathologic anatomy of fibrous dysplasia is discussed at length. Evidence is presented which suggests that so-called ossifying fibroma and non-osteogenic fibroma of bone are variants of this condition. The monostotic form of fibrous dysplasia is not a congenital anomaly, and etiologically has probably nothing in common with the form of polyostotic fibrous dysplasia found in Albright's syndrome. It may represent a disturbance of the normal reparative process following any of a variety of bone injuries.

Infantile Cortical Hyperostoses John Caffey J. Pediat 29 541-599 November 1946

The author adds 6 new cases of infantile cortical hyperostoses to the series previously reported (Am J Roentgenol 54 1 1945 Abstr in Radiology 46 538 1946). The disorder is a new syndrome of unknown cause and obscure pathogenesis. The components of the condition, common to all the cases investigated, are (1) deep swellings of the soft tissues and (2) cortical hyperostoses in the neighboring bones. Other important features include fever, hyperirritability, pseudo paralysis, dysphagia, and pleurisy. Laboratory findings are anemia, leukocytosis, increased sedimentation rate and excessive serum phosphatase.

Hyperostoses have been demonstrated in the mandible and the clavicles most frequently. The calvarium, scapulae, ribs, and the tubular bones of the extremities have also been affected.

Initial symptoms may appear as early as the third week of life or as late as the twentieth month. Duration of the active manifestations varies from eight weeks to nine months. All patients have recovered. No therapeutic agent has altered the course of the disease.

Among the conditions suggested by the above findings are parotitis, osteomyelitis and tumor of the mandible, septic polyomyelitis, leukemia and rheumatoid arthritis or rheumatic fever.

Each of the author's new cases is discussed individually and is accompanied by roentgenograms and a diagram of the skeleton showing the distribution of the involvement. The result is an excellent survey of an interesting syndrome. M. WENDELL DIERZ, M.D.

Osteochondrodystrophia Deformans (Morquio's Disease) Observations at Autopsy in One Case Nathan H. Einhorn, John Royal Moore, and Leonard G. Rowntree. Am J Dis Child 72 536-544, November 1946

Osteochondrodystrophia deformans or Morquio's disease, is characterized by dwarfism, deformities of the bones of the trunk and extremities, and roentgen evidence of absence of centers of ossification, destruction, rarefaction and proliferation involving all bones, including, directly or indirectly, those of the skull.

The roentgen findings are most helpful in the diagnosis. The epiphyses of long bones are usually irregular, enlarged, flattened, and of varying density, suggesting cellular destruction. The femoral head may be absent, misshapen, or fragmented. The acetabulum and glenoid fossa may be irregular and articulation improper. The diaphyses are thinned and show areas of rarefaction near the ends, and the cortex may be thickened on the side of greatest strain. The small bones of the hands and feet are shortened, with thin cortex, irregularities of epiphyses, and increased trabeculation. The ossification centers for carpals and tarsals are deficient for attained age. The vertebral bodies are flattened and irregular in outline, with rough articular surfaces and frequent wedging. Kyphosis in dorsal and lumbar areas and thickening of intervertebral disks are common. The ribs are wide and flat and the intercostal spaces are narrowed, with anterior protrusion of the sternum of varying degree.

The case reported is of a boy, aged 10, who was observed for several years prior to death. He had developed slowly had many deformities typical of the disease, and at the age of four had lost control of the sphincters and leg muscles, so that he was confined to bed thereafter. Roentgen studies showed bone changes typical of the disease and, in addition, changes in the upper cervical region and base of the skull similar to those of platybasia.

At autopsy, the posterior cranial fossa was elevated. The upper cervical vertebrae were fused and there was anteroposterior compression of the spinal cord to the level of the fourth cervical vertebra, with microscopic evidence of extensive vacuolation, loss of horn cells, and much glial proliferation. The compression undoubtedly accounted for the neurologic changes observed.

This disease apparently has two phases, first, the structural defects with postural changes and orthopedic deformities, second, the phase in which the neurologic changes become apparent.

BERNARD S. KALAJIAN, M.D.

Bone Lesions in Early Syphilis Report of a Case Aaron M. Lefkowitz and Kenneth R. Cross. Am J Clin Path 16 693-700 November 1946

A case of early syphilis with widespread involvement of bone in a young white male is presented.

A 22-year-old soldier was treated for malaria in an army hospital in December 1944. The blood Kahn reaction was negative at that time. In January, April and May 1945, recurrences of malarial fever developed and were treated promptly and successfully with atabrine. In May the patient complained of headaches, a "knot" on his head, pain and swelling over the sternum of three weeks' duration becoming progressively worse and a dull aching pain in the region of the right scapula. Examination showed localized swollen

these same measures produce a result with relief of symptoms. The treatment of a fully developed paralytic ileus consists of the use of the Miller-Abbott tube and replacement therapy. In cases where the tube cannot be passed or does not go beyond the pylorus, introduction may be made through a jejunostomy.

MAX CLIMAN, M.D.

A Case of Diverticulosis of the Vermiform Appendix Roentgenographically Demonstrated. John H. Gilmore and Thomas K. Mahan. *Am J Roentgenol* 56:748-750, December 1946.

Diverticulosis of the appendix is seen occasionally by the pathologist but is rarely demonstrated preoperatively. The authors report a case in which appendiceal diverticula were demonstrated on gastro-intestinal examination and later confirmed at surgery.

The patient, a white soldier, aged 25, was admitted to the hospital because of right lower quadrant abdominal pain which had recurred at intervals for two years. There was tenderness in the region of the cecum, most marked over McBurney's point. Rectal examination revealed a small tender mass in the cecal region. No other abnormal symptoms or physical findings were elicited. Routine blood and urine examination showed essentially normal findings. The blood Kahn reaction was negative.

On barium enema examination the colon filled readily, with slight irritability of the ascending colon. A small rounded projection defect extended from the appendix at the junction of middle and distal thirds and was considered to represent a small diverticulum. Another more questionable, diverticulum was seen adjacent to it. Examination twenty-four hours following ingestion of an opaque meal permitted incomplete visualization of the appendix. The appendix extended obliquely upward from the cecal tip and was apparently somewhat fixed in this position.

At operation the cecum was found to be fixed. The appendix was retrocecal, retroserosal and fixed.

Gross examination of the removed appendix showed the serosal surface to be slightly congested but smooth and glistening. Along the medial concave border there were three distinct nodular bulgings, each attached to the appendix along a broad base 6 to 8 mm. in diameter. Incision of the bulgings showed the distal two to have a lumen which communicated freely with the lumen of the appendix. The third showed only a narrow slit-like lumen. On microscopic examination the appendix showed little evidence of inflammatory reaction. The muscular coat of the appendix did not extend completely through the diverticula. A distinct muscularis mucosae was present however and was continuous with the muscularis mucosae of the appendix proper.

The patient made an uneventful recovery.

H. H. WRIGHT, M.D.

THE MUSCULOSKELETAL SYSTEM

Fibrous Dysplasia of Bones. Albert W. Mann, Oliver Eitzen and E. P. McNamee. *Am J Roentgenol* 56:707-711, December 1946.

Fibrous dysplasia of the skeleton has been generally recognized as an entity only since 1937, although it had been known earlier under such names as osteitis fibrosis cystica congenita and precocious puberty and bone brittleness. In addition to bone lesions

there may be such extraskeletal changes as cutaneous pigmentation, somatic precocity in both sexes, and endocrine dysfunction, chiefly in female patients.

While the etiology of the condition is obscure, it is usually attributed to a developmental defect. It is discovered in childhood or early adolescence, a pathological fracture or a limp with pain and deformity of the lower limbs being a frequent complaint. Facial asymmetry, ocular proptosis and acromegalic changes may occur. Laboratory examinations are frequently negative, but the blood phosphatase may be elevated. One or more bones may be involved. There is a strong tendency for the skeletal involvement to be unilateral. The characteristic bone lesions are scattered areas of rarefaction, areas of increased density and overgrowth of bone being less common. The cortex is thinned, and the medullary space distended. Bowing of the long bones and coxa vara may be present. The rarefied areas in the bones are usually composed of collagenous connective tissue in which there may be small foci of ossification.

The condition is self-limited and becomes quiescent in adults. Treatment consists chiefly in measures to avoid spontaneous fractures by guarding against trauma and severe exercise.

The authors report a case of fibrous dysplasia of bone in a boy aged 11 who presented only skeletal manifestations of the disease. He showed involvement of the right femur and both forearms, with pathological fractures. The skull was also involved with marked thickening of the occipital and left parietal bone, associated with sharply defined areas of rarefaction. The left femur showed bowing, with coxa vara, and the left tibia and fibula were affected.

Most of the laboratory findings were within normal limits. However, repeated blood urea determinations varied from 43 to 48 mg. per 100 c.c. and the creatinine ranged from 2.4 to 3.5 mg. per 100 c.c. The blood phosphatase was 5.28 Bodansky units.

A biopsy taken from the left tibia showed abnormal bony tissue occurring as islands in collagenous connective tissue. Occasional osteoblasts and very few osteoclasts were present. No cartilage was identified.

H. H. WRIGHT, M.D.

Fibrous Dysplasia of Single Bones (Monostotic Fibrous Dysplasia). Hans G. Schlumberger. *Mil Surgeon* 99:504-527, November 1946.

This paper is based on 69 cases of fibrous dysplasia which were studied at the Army Institute of Pathology. The lesion was confined to a single bone in 67, involved both the right femur and tibia in one and was polyostotic in another. The ribs were involved in 29 cases, the femur in 9, tibia 8, maxilla 7, calvarium 5, mandible 2, humerus 2, ulna 2, vertebra 1, pelvis 1, fibula 1.

The first sign of the disease was usually a local swelling, particularly if the affected bone was superficial, e.g., the skull, ribs and tibia. Local tenderness was sometimes associated with the swelling and occasionally when one of the long bones was involved, pain of an arthritic character was referred to the nearest joint. In 4 cases the lesion was not suspected until the patient suffered a pathologic fracture. Of the 29 rib lesions, 12 were incidental findings on routine chest films. In contrast to many of the reported cases of polyostotic fibrous dysplasia, none of the cases of the monostotic form showed areas of abnormal skin pigmentation or evidence of endocrine disturbance.

Primary Liposarcoma of Bone. Report of a Case
Herman B Williford and Thomas J Fetherree U S
Nav M Bull 46 1750-1755 November 1946

A diffuse bone tumor involving the pelvis with metastases to regional lymph nodes and the chest, is recorded. The patient, a 31-year old seaman, was admitted to the hospital complaining of pain and stiffness in the lumbosacral area first noticed several weeks previously, when lifting an aircraft propeller. Subsequently, coughing or straining produced a momentary sharp pain in the lower lumbar area. About four days prior to admission a dull generalized lumbosacral pain developed following the onset of a cold. The patient complained also of weakness of a month's duration and a loss of about 15 pounds over the past several months.

Examination of the blood showed an anemia (hemoglobin less than 7.5 gm per cent, red blood cells 1,600,000) which appeared to be of a hypochromic, microcytic type. Roentgenograms of the dorsal and lumbar spine, the skull, and both thighs and legs were within normal limits. An intravenous pyelogram was likewise essentially normal. Prominent markings were present throughout the entire right lung, but there was no definite evidence of metastasis or parenchymal infiltration. Stereoscopic studies of the pelvis showed a diffuse irregularly distributed predominantly osteolytic lesion involving the sacrum, the upper two-thirds of the ilium bilaterally and, to a lesser extent, both pubic bones. Irregular areas of osteoblastic activity were associated with the bone destruction. The osteolytic and osteoblastic processes combined to give the bone a mottled appearance. These findings were interpreted as metastases of undetermined origin.

The patient was treated symptomatically and attempts were made to combat the anemia. In one month the red blood cells numbered 3,050,000 and the hemoglobin 9.5 gm per cent. A chest film now revealed a moderately large convex shadow at the left hilum, which was interpreted as a metastasis to the hilar nodes. Throughout the medial two-thirds of the right lung field was a very fine parenchymal infiltration, with peribronchial distribution. In the lower half of the lung there was some confluence of these linear areas of infiltration with the formation of small areas of consolidation. No bony metastasis was noted in the thorax.

During the next month the patient slowly lost ground and death followed a cerebrovascular accident two months after admission. An autopsy was performed. Microscopic examination revealed neoplastic tissue in the bone marrow, lymph nodes, lungs, and right kidney. Pathologically the lesion was considered to represent primary liposarcoma of bone.

The x-ray findings in the bone in this case presented no particular features which might not be produced by a predominantly osteolytic metastatic carcinoma. The lesion was so interpreted initially, and a review of the films following postmortem examination brought out no features which would lead to a different interpretation. Should a similar situation be encountered. The chest findings also presented no peculiarities which would give a clue as to the nature of the underlying metastatic tumor.

Skeletal Lymphosarcomatosis with Secondary Hyperparathyroidism A. von der Sar and P. H. Hartz. Am J Clin Path 16 701-713 November 1946

A case of hyperparathyroidism secondary to skeletal lymphosarcomatosis in a 55-year-old Negro male is re-

ported. The patient was admitted to the hospital with a diagnosis of rheumatoid arthritis or syphilis. He complained of pain in all extremities and of dull headache for six months. He had been bedridden for two months. His joints were painful but not swollen and walking was difficult. The skull appeared to be getting softer and smaller in circumference. In the last eight months all of the teeth had fallen out. There were no urinary symptoms.

The patient was emaciated, weighing only 92 pounds. The head was very tender to palpation, much of the calvarium had disappeared, and only a soft mass could be felt. The cervical lymph nodes were not palpable and the thyroid was not enlarged. The chest was painful to palpation. The fingertips of both hands were slightly enlarged and the nails had the appearance of a parrot's beak. Wassermann and Kahn tests were negative. Serial chemical examination showed a hypercalcemia. The phosphorus content of the blood serum was low. Roentgenograms showed severe decalcification of the whole skeleton, the lesions closely resembling those of osteitis fibrosa and metastatic tumor. Except for small areas in the tibiae and heads of the fibulae the distal ends of the extremities were atrophied. Urinalysis during a constant low calcium diet showed a high excretion of calcium and inorganic phosphorus. A tentative diagnosis of hyperparathyroidism was made on the basis of chemical examinations. Biopsy of a rib supported this diagnosis.

A quick deterioration in the patient's condition, with an irregular fever and uremic symptoms, made an exploratory operation impossible for some time. When it was finally undertaken the parathyroids were found to be slightly enlarged and of normal number. No adenoma could be detected. One left and two right glands were removed. The patient died in uremia.

Necropsy revealed diffuse lymphoid tissue consisting of small and medium sized lymphocytes in the tonsils, lymph nodes, calvarium, dura and periosteum. The authors believe, therefore, that a diagnosis of lymphosarcomatosis with cranial metastasis is warranted. There was an extensive absorption of bone by osteoclasts and replacement of normal marrow by connective tissue rich in collagen and containing lymphocytes and multinucleated giant cells. These findings, together with the results of the biochemical and roentgen examinations, are typical of osteitis fibrosa. The presence of lymphocytic infiltrates in the fibrous marrow may be considered as a chronic inflammatory reaction or as a beginning infiltration with neoplastic cells; the authors favor the first view. The calcification in the lungs and kidneys found at autopsy must be regarded as a sequel of the osteitis fibrosa.

The parathyroid glands were only slightly enlarged and consisted almost exclusively of principal cells. On the basis of these findings the histologic findings on biopsy of the rib, the hypercalcemia, the low phosphorus content of the blood, and the high excretion of calcium and phosphorus in the urine, a hyperparathyroidism is believed to have existed. This was probably secondary to a disturbance of the calcium metabolism caused by metastatic skeletal lymphosarcomatosis.

Pyogenic Osteomyelitis of the Spine Peter Martin
Brit M J 2 683-691 Nov 9, 1946

Osteomyelitis of the spine forming part of a generalized bacteremia has usually been a fulminating infec-

areas over the right fronto-parietal the parietal, and temporoparietal regions of the skull and over the right costosternal junction at the level of the second rib. These swollen areas varied in size from one half inch to one inch in diameter and were tender on pressure. X-ray examination of the skull on May 28 showed a small tumor in the soft tissue of the scalp on the right side just anterior to the coronal suture about 4 cm lateral to the sagittal suture. There was slight erosion of the outer table of the skull at the site of the tumor. The sedimentation rate was 44 mm in one hour. The complaints referable to the skull and sternum continued and the pain in the right scapula became worse. Films taken on June 1 showed an increase in the size of the lesions noted on May 28. There was no bony involvement of the sternum and right scapula. On June 20 the blood Kahn and Kolmer reactions were positive. On June 30 X-ray examination showed a slight increase in the size of the areas of erosion in both the right and left frontal and the right parietal bones. One of these areas appeared to penetrate the inner table of the skull. On July 23 several irregular areas of alopecia over the occipital and parietal regions were observed. X-ray examination of the bones of the left upper extremity, both lower extremities, and pelvis showed no abnormalities.

On July 6 the largest skull lesion was curetted. Histologic examination showed granulomatous tissue with some focal distribution of inflammatory infiltration. Actual caseation was absent but slight degeneration associated with active fibroplasia and osteogenesis was evident. There was only moderate endothelial hyperplasia. These changes represent one phase of syphilitic osteomyelitis. A lymph node removed from the left inguinal region showed multiple small granulomata and generalized lymphoid and reticuloendothelial hyperplasia commonly seen during the secondary stage of syphilis.

At first the positive blood reaction was thought to be a false positive because of the coexisting malarial infection. The true nature of the disease was recognized only after histologic sections of bone and lymph node were examined. The diagnosis was confirmed by quantitative serologic studies at the Army Medical Center. Although the patient had no demonstrable primary luetic lesion it is believed that he acquired syphilis during a furlough in March. The tender swollen areas on the skull were first noticed approximately four to six weeks after sexual exposure, or well within the period of secondary stage. The paroxysms of chills and fever due to the recurrent vivax malarial fever had no effect upon the invasive ability of the spirochetes. The patient made an excellent response to penicillin.

Some Observations Concerning Ewing's Tumor Seen in an Army General Hospital. Gilbert W. Heublen, Sylvan E. Moolten, and Joseph C. Bell. *Am J Roentgenol* 56: 688-703, December 1946.

The clinical features, histopathology, diagnosis, and treatment of Ewing's tumor are discussed and 7 cases illustrating various aspects of the disease are presented.

Of 30-42 admissions to the Percy Jones General Hospital 55 were for bone tumors 24 of which were malignant 10 representing Ewing's tumor. The incidence of bone tumors was unusually high because this hospital was both an amputation and deep roentgen therapy center. Reports from large civilian hospitals

show a much lower ratio of bone tumors to admissions.

Ewing's tumor occurs most often in young persons between the ages of five and fifteen, and 3 out of 4 cases occur in males. The 'pipe' bones are the most frequent sites especially the tibia, fibula, humerus, ulna, and femur. The clavicles, tarsal bones, ribs, vertebrae, mandible, skull, shoulder girdle, and pelvis are also occasionally involved. The most frequent clinical findings are (1) history of trauma, (2) intermittent symptoms of pain and fever, (3) a mistaken diagnosis of chronic osteomyelitis in the case of long bones or of tuberculosis in the presence of vertebral involvement. Joint involvement is rarely seen. Considerable local hyperemia may be present adding to the difficulty in distinguishing this condition from osteomyelitis.

The histogenesis of Ewing's tumor is a subject upon which there is much disagreement. Basically the tumor consists of solid cords of rounded cells separated by fibrous bands. Delicate reticulin fibers may exist between individual tumor cells or may be absent. The nuclei are rounded and the cell outline is indistinct. There is a marked uniformity in the appearance of the cells. One of the most characteristic features is the absence of intercellular substance. The cells are two to four times the size of a small lymphocyte. Some maintain that it is impossible to separate reticulum-cell sarcoma and Ewing's tumor and that the two are variants of the same condition. The cell of origin has been considered by some to be the undifferentiated mesenchymal cell which in postnatal life is found about small blood vessels and capillaries. Differentiation of this cell along various lines, according to this opinion, could produce fibrosarcoma, osteogenic sarcoma, and lymphoblastoma. Because of the constant association of this tumor with a bone locale it seems necessary to relate the tumor in some manner to osteogenic mesenchyme. The authors consider the tumor an embryonal osteoblastoma, non-osteogenic.

The clinical findings, roentgenographic study and histopathologic examinations are all important in making the diagnosis of Ewing's tumor. The roentgenogram will ordinarily indicate whether the tumor is intrinsic or extrinsic in relation to the shaft, whether it is benign or malignant and the extent of involvement. In some instances the tumor type may be accurately determined. Occasionally the roentgen findings may be more diagnostic than the pathologic report based on insufficient biopsy material. Osteomyelitis is the condition most likely to be confused with Ewing's tumor. Any obscure lytic changes in bone or minimal periosteal proliferation should be followed by serial roentgenography and early biopsy. Ewing's tumor occurring in the sacrum is particularly difficult for differential diagnosis. One should remember that in Ewing's tumor there may be spontaneous decrease in the size of the lesion. The presence of intercurrent disease, such as syphilis, may be a confusing factor.

Where the diagnosis of Ewing's tumor is suspected but cannot be substantiated by biopsy, the therapeutic test is valuable. Small doses of 100 to 150 r will often cause rapid regression of the tumor and relief of pain after only a few treatments. With other osteogenic tumors relief of pain does not ordinarily occur with moderate amounts of roentgen therapy or the analgesic effect is delayed for a matter of two weeks or more.

Treatment is primarily surgical and the use of deep roentgen therapy alone is not warranted except where the lesion is inoperable. H. H. WRIGHT, M.D.

ated anterior or slightly anterolateral to the nerve root cause a defect in the filling of the root pouch without disturbing the thecal column. When the prolapse is situated further laterally the myelogram may show a characteristic change or it may remain normal.

The question of intermittent prolapses is discussed in detail. These are the "concealed" disks described by Dandy (J A M A 117 821, Sept 6 1941). The authors employ extension of the spine to demonstrate the prolapse by myelography and also at operation.

Extrusions may displace root pouches and they may cause defects in the thecal column at a distance from the disk space.

Scarred disks can be identified by plain films in conjunction with myelography. The indentation in the myelogram coincides with the bony spurs and is not caused by soft tissue protrusion. Many scarred disks of this type are asymptomatic.

The indirect effects of disk prolapse are swollen intrathecal nerve roots and arachnoiditis. The latter is identified by a serrated edge produced by seepage of medium between the neighboring roots of the cauda equina matted together with adhesions. Hypertrophy of the ligamentum flavum has not been found at operation, and the authors believe that the myelographic appearance adduced by other authors as evidence of this condition is to be explained by disk lesions alone.

Artefacts may give rise to misleading appearances and render the myelogram worthless. These may be produced by the medium leaking into the subdural space into the extradural tissues and along the epidural spaces. To prevent these conditions, lumbar puncture should be performed with the patient lying horizontal and the injection should not be made within several days of a previous spinal puncture.

In 80 cases of this series satisfactory myelograms were obtained, and of these 76 were interpreted as pathological while 10 (12 per cent) were considered normal. In all except 1 case one or more disk lesions were subsequently established at operation. In each of the 10 cases with negative myelograms a disk lesion was present at operation. In 74 cases the presence and level of a disk protrusion were indicated with almost complete accuracy. In this series a third of the prolapses were centrally placed while two thirds were laterally placed.

A large number of excellent reproductions of myelograms illustrate the various types of disk lesions found by the authors.

MAX CLIMAN, M.D.

Congenital Bipartite Carpal Navicular Thomas F. Rose. *Australian & New Zealand J Surg* 16 149-151 October, 1946.

Rose cites the case of a 37 year-old soldier who sustained an injury to the right wrist and subsequent x-rays were interpreted as an ununited fracture of the navicular. Studies of the left wrist disclosed similar findings despite a negative history of trauma. Because the physical findings and roentgenograms were not indicative of a carpal fracture, a diagnosis of a tear of the volar radio-carpal ligament was made, associated with bilateral bipartite navicular carpal. The patient's recovery was complete and films taken at a later period disclosed an unchanged appearance of the bipartite naviculars.

A true bipartite navicular is divided across the wrist into more or less equal portions. There is a joint space between the fragments which communicates with the

carpal joint system, but is separated from the radio-carpal joint by a ligament uniting the proximal edges. The dividing line extends obliquely from the outer end of the articulating surface of the radius to about the middle of the concave surface of the head of the capitate. This condition is commonly bilateral, though unilateral cases have been reported.

The author stresses points in differential diagnosis. The prevailing criteria, lack of trauma, lack of disability, and a bilateral lesion are considered insufficient evidence on which to base a diagnosis of bipartite navicular. Despite slight and perhaps forgotten trauma and minimal disability x-ray studies may demonstrate an ununited fracture of the navicular.

The final diagnosis is therefore solely dependent upon the radiologic findings. The bone texture of each fragment of a bipartite navicular is normal and of equal density. The apposing edges of the fragments are smooth and thin, and there is no evidence of osteoporosis or osteosclerosis. Should there be any change in bone texture such as irregularity or increased density in the line of demarcation, then the separation must be regarded as a fracture, even though the condition is bilateral and the patient cannot recall injury.

LOUIS BERNSTEIN, M.D.

Para-Articular Calcification in the Lower Extremities of Paraplegic Patients William C. Ward. *Am J Roentgenol* 56 712-715, December 1946.

Calcification about the joints and in the soft tissues of the lower extremities of paraplegic patients has been reported infrequently. Previous reports are mainly from the European literature and indicate that the condition had been observed in veterans of World War I who had sustained spinal cord injuries.

The author observed 88 patients with spinal cord and cauda equina injuries of varying severity. Only 33 of these were seen for any considerable period. Para-articular and soft-tissue calcification in the lower extremities was observed in 4 of these patients but as only those patients with swelling or stiffness of the joints were completely studied by roentgenograms the actual incidence is unknown. Three of the patients had only a minor degree of calcification about the knee joints. The fourth had extensive calcification about the knees and in the soft tissues of the lower thighs.

This last patient, a 26-year-old soldier, sustained a shell fragment wound of the spine at the level of the 10th thoracic vertebra. A lumbar puncture on the following day revealed complete block of spinal fluid. During the ensuing week massive edema of both lower extremities developed and within a month large decubitus ulcerations were present over both hips and the sacrum. Roentgenograms of the lower extremities made approximately eleven weeks following the injury showed extensive calcification in the soft tissues about both knee joints. With supportive therapy the edema of the legs was reduced, and the decubitus ulcers improved. Fine granular deposits of calcium were noted in the soft tissues of the right hip region approximately six months following injury. At eleven months there was some fragmentation of the articulating surface of the head of the femur, with marked para-articular calcification.

It appears that calcification about the joints and in the soft tissues usually begins during the first year after spinal cord injury, if it is to develop except in those cases that have late associated fractures. The cause of

tion, fatal in a high percentage of cases. Antemortem diagnosis has not often been made. When, however, the disease is localized, the mortality may be as low as 25 per cent. Martin believes that many so-called cases of spinal tuberculosis which heal rapidly with early fusion may in reality be pyogenic osteomyelitis and their inclusion would reduce the mortality still further.

Pyogenic osteomyelitis of the spine is more common in males (3 to 1) and the usual age of onset is in the third decade in contrast to the earlier occurrence of osteomyelitis elsewhere. The most common infecting agent is *Staphylococcus aureus*, while *Staphylococcus albus* and *Streptococcus* are more rarely responsible. The lumbar region is most frequently involved. The bodies of the vertebrae are generally affected as a metastatic phenomenon, the primary focus being in a boil, tooth infection, septic wound or other suppurative process.

Pathologically an ulcerating lesion showing a tendency to spread to adjacent segments is produced. The disk cartilage is rapidly destroyed early in the process, and the infection then attacks the next vertebral body. This is in contrast to tuberculosis in which the disk is not so readily destroyed and spread of the infection to adjacent vertebrae is under the anterior spinal ligament rather than through the disk. Abscesses often occur and may point along fascial planes producing retropharyngeal, mediastinal, psoas, perinephritic, or pelvic abscesses depending on the portion of the spine involved. Sinus formation is not uncommon. Abscess may be present with minimal bone involvement. Epidural abscess with compression of the cord or meningitis occurs infrequently but carries a high mortality.

The onset is often acute with local signs obscured by the intensity of the toxemia. Spontaneous lumbar pain, diffuse at first and later localized, is often severe enough to confine the patient to bed. It is accompanied by muscular spasm and signs of toxemia.

Radiologically little may be found in the fulminating cases. In the subacute infections as the disease attacks the vertebral body it may be two to three months before x-ray changes are demonstrable. Narrowing of the intervertebral space with moth-eaten irregularity of the adjacent bony surfaces is the first change. Increased density of the affected vertebral body with areas of mottled rarefaction, is common. Subperiosteal new bone is formed at the edges of the contiguous vertebrae leading to a beaking which continues to increase in size and eventually fuses producing bony ankylosis. This may occur in seven months or more.

The differentiation from tuberculosis may be difficult but the acute onset, the early cartilage destruction, the signs of toxemia, and the absence of collapse of the vertebral body are usually diagnostic. Five illustrative case reports are presented. The treatment is bed rest with support, a plaster jacket, general measures including the use of penicillin and other medication and surgical drainage of abscesses when formed.

BERNARD S. KALAJIAN, M.D.

Myelography in Lumbar Intervertebral Disk Lesions. A Correlation with Operative Findings. A. Charles Begg, Murray A. Falcoer and Murray McGeorge. *Brit J Surg* 34: 141-157, October 1946.

On the basis of operative and myelographic experience the authors divide disk lesions into four separate groups, as follows: (1) a constant, localized projection of nucleus substance still covered by the smooth

glistening annulus fibrosus thinned but intact; the commonest type, (2) an intermittent prolapse, occurring only when the intervertebral disk is subjected to certain strains, (3) extrusions, due to rupture of the annulus fibrosus and escape of nuclear material into the spinal canal, (4) scarred disks in which over a period of years, the opposing surfaces of the vertebral bodies become sclerotic, the disk space is diminished in width, and the theca and extrathecal nerve root become adherent to the back of the disk without an actual projection.

Myelography, employing either pantopaque or lipiodol, was carried out in 95 of 100 consecutive cases of sciatica and low back pain. The method of examination is described in detail and differs very little from that employed by most authorities. With hyperextension of the spine it was found possible to demonstrate lesions which the usual technique failed to disclose. Lipiodol was aspirated at operation after the theca had been opened. Pantopaque was often left *in situ* and no harmful effects were noticed. This permitted re-examination at intervals after the initial myelogram. Follow-up radiological studies have shown that pantopaque is slowly absorbed, approximately two-thirds of its volume in a year.

The anatomical considerations in relation to myelography are discussed in detail, with excellent illustrations. The first sacral nerve roots emerge from the theca at or just below the 5th lumbar disk. The 5th lumbar nerve roots emerge at or just below the 4th lumbar disk, while nerve roots higher up all emerge below the disk cephalic to their numerically corresponding vertebra. Consequently disk protrusions situated posterolaterally at the 4th and 5th lumbar spaces readily compress the 5th lumbar and 1st sacral nerves, respectively, while similar protrusions at higher levels usually do not involve an extrathecal nerve root.

The normal myelogram is well described under two headings: the thecal column and the root pouches. The optimum amount of medium is 3 c.c., this amount, when collected along the anterior wall of the lumbar theca, forms a pool which is usually sufficient to straddle one disk space at a time but not two. The width of the thecal column may vary from 30 to 80 per cent of the interpedicular distance. The filling of the root pouches will depend on time, gravity and the posture of the patient.

Disk prolapses are divided into central and lateral groups according to their location in the coronal plane. Central prolapses lie anterior to the theca, while lateral protrusions lie between them and the intervertebral foramen. If a central prolapse is large enough, a complete block will result but this is uncommon. With medium sized prolapse the usual finding is an hour glass constriction of the thecal column. Prone lateral views of these hour glass constrictions have invariably disclosed an anterior invagination of the thecal column confirmed by operation. The authors do not believe that hypertrophy of the ligamentum flavum produces this deformity. A less common appearance with a medium sized prolapse is a rounded zone of radiolucency lying within the thecal column and causing no deformity of its margins in the anteroposterior view. The anterior invagination can be detected only in the prone lateral projection. When a prolapse occurs in relation to an extrathecal nerve root, there will be a defect in the lateral border of the thecal column while the corresponding root pouch usually fails to fill. Lesions situated

ated anterior or slightly anterolateral to the nerve root cause a defect in the filling of the root pouch without disturbing the thecal column. When the prolapse is situated further laterally the myelogram may show a characteristic change or it may remain normal.

The question of intermittent prolapses is discussed in detail. These are the "concealed" disks described by Dandy (J A M A 117 821 Sept 6 1941). The authors employ extension of the spine to demonstrate the prolapse by myelography and also at operation.

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carpal joint system, but is separated from the radio-carpal joint by a ligament uniting the proximal edges. The dividing line extends obliquely from the outer end of the articulating surface of the radius to about the middle of the concave surface of the head of the capitate. This condition is commonly bilateral, though unilateral cases have been reported.

The author stresses points in differential diagnosis. The prevailing criteria lack of trauma, lack of disability, and a bilateral lesion are considered insufficient evidence on which to base a diagnosis of bipartite navicular. Despite slight and perhaps forgotten trauma and minimal disability, x ray studies may demonstrate an ununited fracture of the navicular.

The final diagnosis is therefore solely dependent upon the radiologic findings. The bone texture of each fragment of a bipartite navicular is normal and of equal density. The apposing edges of the fragments are smooth and thin, and there is no evidence of osteoporosis or osteosclerosis. Should there be any change in bone texture, such as irregularity or increased density in the line of demarcation, then the separation must be regarded as a fracture, even though the condition is bilateral and the patient cannot recall injury.

LOUIS BERNSTEIN M D

Para-Articular Calcification in the Lower Extremities of Paraplegic Patients William C Ward Am J Roentgenol 56 712-715, December 1946

Calcification about the joints and in the soft tissues of the lower extremities of paraplegic patients has been reported infrequently. Previous reports are mainly from the European literature and indicate that the condition had been observed in veterans of World War I who had sustained spinal cord injuries.

The author observed 88 patients with spinal cord and cauda equina injuries of varying severity. Only 33 of these were seen for any considerable period. Para-articular and soft-tissue calcification in the lower extremities was observed in 4 of these patients but as only those patients with swelling or stiffness of the joints were completely studied by roentgenograms, the actual incidence is unknown. Three of the patients had only a minor degree of calcification about the knee joints. The fourth had extensive calcification about the knees and in the soft tissues of the lower thighs.

This last patient, a 26-year-old soldier, sustained a shell fragment wound of the spine at the level of the 10th thoracic vertebra. A lumbar puncture on the following day revealed complete block of spinal fluid. During the ensuing week massive edema of both lower extremities developed and within a month large decubitus ulcerations were present over both hips and the sacrum. Roentgenograms of the lower extremities made approximately eleven weeks following the injury showed extensive calcification in the soft tissues about both knee joints. With supportive therapy the edema of the legs was reduced and the decubitus ulcers improved. Fine granular deposits of calcium were noted in the soft tissues of the right hip region approximately six months following injury. At eleven months there was some fragmentation of the articulating surface of the head of the femur with marked para articular calcification.

It appears that calcification about the joints and in the soft tissues usually begins during the first year after spinal cord injury if it is to develop except in those cases that have late associated fractures. The cause of

the calcification is not known. Multiple minor traumas have been considered a predisposing factor. Edema of the extremities is a fairly frequent finding shortly after spinal cord injury due to immobilization, vasomotor relaxation, nutritional hypoproteinemia, and other factors. Patients who have been observed to have even minor degrees of soft tissue and par-articular calcification have had massive edema of the lower extremities following the spinal cord injury. There is rapid demineralization of the bones of the lower extremities with associated hypercalciuria. The calcification about areas of fractures that have occurred late after spinal cord injury is related to trauma and hemorrhage into the soft tissue.

Extensive calcification about the knee or hip joints may interfere with the rehabilitation of the paraplegic patient. No treatment has been recommended for the condition. Prevention of fracture which might result from too vigorous efforts at rehabilitation is emphasized.

H. H. WRIGHT, M.D.

Avulsion Fracture of the Eminencia Intercondylar in the Knee Joint. F. Jakob. *Schweiz med. Wchnschr.* 76: 1230-1231. Nov. 30, 1946.

Avulsion fracture of the tibial spine is a result of pull on the cruciate ligaments. The fracture may be found in association with fracture of the tibial condyle. The injury is commonly sustained during a ski run. The external mechanism is either forcible external rotation with abduction, or else hyperextension. The diagnosis is seldom made clinically because of gross distortion of the joint from the accompanying hemarthrosis; there is no sign pathognomonic of ligament injury and a conclusive diagnosis of fracture can be made only by roentgen study. The fracture may vary from the faintest fissure to gross avulsion of the top of the tibial spine. In severe cases there is often a tendency to lateral displacement of the tibia, usually of slight degree.

Therapy should be conservative, generally plaster immobilization. Operation is reserved for cases of severe dislocation or displacement of the fragment with symptoms of joint mouse and in these removal rather than replacement of the fragment is recommended. Results are usually good, occasionally a slight limitation of flexion remains.

LEWIS G. JACOBS, M.D.

GYNECOLOGY AND OBSTETRICS

Pelviography. D. Jefferiss and Eric Samuel. *Brit. J. Radiol.* 19: 462-468. November 1946.

Pelviography was first described by Kjellberg in 1942. The present paper presents the results in 21 patients. A water soluble opaque medium is injected by a technic similar to that used in uterography but in addition to filling the uterus the solution is allowed to flow through the tubes into the pelvis. The authors use 20 to 30 c.c. of any preparation suitable for intravenous pyelography after diluting it with 10 to 15 c.c. of 0.5 per cent novocaine. The injection is made under fluoroscopic control.

An anteroposterior film is made as soon as the uterine cavity and the tubes are filled. The solution is then allowed to flow through the tubes into the pelvic cavity and three more films are made: an anteroposterior and a right and left lateral with the patient on her side and the beam horizontal. Since the shadow of the medium is not very dense careful radiographic technic is required.

No complications were encountered. The catheter could not be passed into the cervical canal in 3 cases. Pain was severe in one patient and slight in two.

The appearance of the uterine cavity and tubes is the same as with opaque oils. In the pelvis, the dye accumulates in Douglas' pouch and spreads out, outlining the solid structures in the pelvis and also coating the bowel. The latter sometimes produces confusing shadows but can usually be identified.

In hydrosalpinx the dye usually enters the dilated tube and mixes with the contained fluid producing an oval opacity with a moderately clear outline situated along the line of the fallopian tube, often showing a fluid level or stratification. Cystic ovarian tumors can usually be readily recognized. General thickening of the uterine wall can be seen and pedunculated fibroids on the peritoneal surface can usually be diagnosed. Tumors of the broad ligaments may be visualized. Occasionally inflammatory adhesions may be seen but in inflammatory disease the tubes are frequently occluded.

SYDNEY J. HAWLEY, M.D.

THE GENITO-URINARY SYSTEM

Arteriography in Renal Diagnosis. Preliminary Report and Critical Evaluation. Frederick B. Wagner, Jr. *J. Urol.* 56: 625-635. December 1946.

The author's object is to stimulate further interest in arteriography as an aid to renal diagnosis by description of a simplified technic, critical evaluation of the procedure and presentation of three cases.

After preliminary anesthesia the twelfth rib on the left side is palpated. With a short stout needle the skin is punctured just below this rib, four fingers' breadth from the spinous processes. A 15-cm. needle is then introduced through the puncture hole and directed anteriorly, medially and cephalically toward the body of the twelfth thoracic vertebra. When bone is encountered, the needle is withdrawn about 2 cm. and the point directed more laterally so as to just pass by the vertebral body. The stylet is then removed and the needle cautiously advanced to within a few centimeters of its hilt. The aortic wall is encountered as a resistance through which the needle snaps, imparting to the operator a sensation similar to that experienced in penetrating the dura mater during a spinal tap. Almost immediately bright red blood emerges from the needle as a pulsating drip which descends as a rivulet on the shaft.

The needle is then connected to the rubber tubing and syringe which have been previously filled with sterile salt solution. Barbotage is carried out to note the ease of flow in both directions. A trial injection of 12 c.c. of saline solution within six seconds is made in order to estimate the force required. The stopcock is then closed, the syringe disconnected and filled with approximately 12 c.c. of 80 per cent sodium iodide solution. The syringe is again connected, the stopcock opened and blood withdrawn as a final proof that the needle is well within the lumen. The signal ready is given to the x-ray technician, the solution is injected at the rate of 2 c.c. per second and the signal "shoot" given as the final cubic centimeter or two leave the syringe. Immediately following exposure of the roentgen film the needle is withdrawn.

The author indicates that this technic is best suited for visualization of branches of the celiac axis and superior mesenteric artery. Visualization of the

renal artery and its branches appears to be better if the needle is inserted one vertebral level lower

Before undertaking abdominal arteriography one should be fully acquainted with the difficulties and potential dangers. In the first place, the patient is exposed to the hazards of anesthesia, acute iodism, extravasation of radiopaque medium, and hematoma following puncture. Secondly, the operator must acquire a thorough knowledge of the relational anatomy involved in the procedure. Aortic puncture should first be practised in the dissecting or postmortem room in order to acquire experience and confidence. Thirdly, the actual technique, though relatively simple, is exacting and demands perfect co-ordination of the team, for the slightest error may yield an unsatisfactory film. Finally, even an excellent arteriogram in some instances may be difficult to interpret accurately because of lack of experience.

The author cites the literature and his own experience (23 aortographies) to indicate that the risk of abdominal arteriography seems no greater than that of arteriography of peripheral vessels. It is his opinion that this type of study is of value as an occasional diagnostic adjunct in carefully selected instances. From the standpoint of renal diagnosis the study may be indicated when all other studies have been exhausted and further information is desired regarding (1) hypertension in which surgical treatment is contemplated, (2) aberrant renal vessels as a possible cause of hydro-nephrosis, (3) renal or adrenal tumors, (4) possible renal aneurysm, (5) suspected aortic obstruction near the renal arteries.

The three cases described include one of hypertension, one of possible renal aneurysm, and one of an unusual renal tumor.

MARLYN W. MILLER, M.D.

Pelvic Single Kidney. Report of a Case. Howard B. Mays. *J Urol* 56: 619-624, December 1946.

Inclusive of the author's case, there are only 41 reported cases in the literature of pelvic single kidney or congenital solitary pelvic renal ectopia.

Urinary symptomatology in the majority of cases is usually insignificant or absent. An associated anomaly of male and female genitalia was found in 20 of the 41 cases. The condition should be considered as a possible diagnosis, and further urologic study should be made, in the presence of an unexplained pelvic mass extrinsic to the intestine as suggested in a gastro-intestinal roentgenographic study, or causing extrinsic pressure on the bladder during cystoscopy or on the bowel during sigmoidoscopy. Bimanual palpation of pelvic masses in male and female may also prove to be of considerable aid in diagnosis.

The author's patient was a 29-year-old white male, who had led a normal active life and at the time of admission to a military hospital had been on active duty in the China India Burma theater for two years and seven months. He was admitted to the hospital complaining of pain in the hypogastrium, fever, and nausea of two days' duration. He had had similar episodes at irregular intervals for four years prior to admission. He had recently been treated for tertian malaria. Examination revealed definite tenderness in the lower abdomen. In the hypogastrium a rounded, smooth, firm mass was palpable extending above the symphysis and to the right of the mid line. The mass was defined, as well on bimanual examination. The genitalia were normal, as were the rectum and prostate. Urinalyses were

negative. Roentgen study of the gastro-intestinal tract showed that the mass was not directly associated with the large or small intestine, though an appendiceal abscess was considered a possibility. The survey abdominal roentgenogram showed no distinct nephric outlines and the psoas muscles were indistinct. Exploratory laparotomy revealed a large ectopic right kidney, with a short renal artery coming off the iliac artery. There was no evidence of another kidney on either side.

Urologic study subsequently was undertaken. Cystoscopy revealed a total absence, with no discernible vestige, of the left half of the trigone. There was no evidence of a left ureteral orifice. The right portion of the trigone was normal and the right ureteral orifice was not unusual. The fundus was asymmetrical. Renal function was considered normal and urine cultures were negative. Retrograde pyelography demonstrated the kidney pelvis over the lower sacrum and slightly to the right of the mid line. The pelvis was small and the ureter short and tortuous. Excretory urograms demonstrated apparently normal function, absence of obstruction and emptying time well within normal limits.

The subjective symptoms suggested recurring obstruction to the flow of urine. However, the objective evidence of interference with urinary output was entirely lacking and surgery was deemed to be contraindicated.

DAVID S. MALEN, M.D.

THE BLOOD VESSELS

A Case of Congenital Multiple Arteriovenous Fistulae of the Hand. J. A. White. *Brit J Surg* 34: 209-211, October 1946.

A girl aged 12 had a purplish discoloration of the right hand, present since birth. Increase in the size of the hand and deformity had been noticed for the past two or three years. Examination revealed a large irregular port-wine stain on both palmar and dorsal surfaces. The whole hand and forearm were covered with dilated veins. The four fingers showed gigantism and deformities. A thrill was palpable in the palm, and with the stethoscope a continuous-cycle bruit with systolic accentuation could be heard over most of the hand but was maximum on the palmar surface at the base of the first finger. No murmur could be heard above the wrist when a tourniquet had been applied at this level, thus proving the arteriovenous communications to be at or below the wrist. The blood pressure in the affected upper arm was 125 systolic and 40 diastolic while in the normal arm it was 95 systolic and 60 diastolic.

X-ray examination of the right hand revealed hyperostosis of the 2d, 3d, 4th and 5th metacarpals, deformity of the radial and ulnar epiphyseal regions, and a patchy sclerosis of the scapular bone as in Kienbock's disease. The shafts of the 2d, 3d, and 4th phalanges showed irregular trabeculations and increased bone striations as seen in hemangioma. An arteriogram showed extensive arterial filling of the palmar arch with accumulation of medium between the heads of the 2d and 3d metacarpals. There was no filling of the thumb area. These findings suggested multiple fistulae and small aneurysmal sacs in the region of the 2d and 3d metacarpophalangeal joints.

Injectations of sclerosing fluid into regional veins had no effect. Four attempts at surgical extirpation gave no

improvement and the patient was discharged. A severe hemorrhage later necessitated amputation through the forearm at another hospital. MAX CLIMAN M.D.

TECHNIC

Persistence of Fluoroscopic Screens Willard W Van Allen. *Pub Health Rep* 61 1583-1588 Nov 1 1946

The luminescence produced in phosphors by exciting visible light, ultraviolet or roentgen rays has long been recognized as of two distinct types (a) fluorescence during excitation, and (b) fluorescence after the exciting radiation has been cut off. Phosphorescent emission is of longer wave length than fluorescent emission, and phosphorescence lasts for an appreciable time after termination of the exciting radiation whereas fluorescence occurs only during excitation. While these mechanisms have been described previously, the exact part they play in diagnostic radiology has not been brought before the radiologist critically. The phenomenon of 'lag' or 'persistence' has been noted but the qualities of different screens has not been

brought out as clearly as in the present paper. There is also another concept which is relatively new and usually not appreciated—in some screens the phosphorescence 'builds up' during successive exposures until it reaches values many times greater than that after a single exposure. With the advent of the photoelectric timer, this persistent phosphorescence causes successive exposures to be prematurely terminated with the result that films are underexposed as well as lacking contrast.

The U S Public Health Service, through Dr Van Allen carefully investigated four screens: Patterson Types B and D and the U S Radium Corporation's 666D and 574A. The screens that have little 'lag' and do not 'build up' under multiple exposures are of course, best. There is, however, considerable difference in the resolving power of the screens. The Patterson Type B shows a slight 'lag' advantage, in resolving power, the U S Radium Corp 666D screen has considerable advantage. [For further observations on screen characteristics see *Morgan Radiology* 49 90 1947—Ed.] SYDNEY F THOMAS M.D.

RADIOTHERAPY

Analysis of 402 Cases of Carcinoma of the Breast. Evelyn Siris and Leonard Dobson. *California Med* 65 201-206, November 1946

In view of the differences of opinion as to the proper treatment in operable breast tumors with axillary involvement, the authors undertook an analysis of 402 cases of breast cancer treated from 1926 to 1945. The classification was in general that of Steintal. Of the 402 cases 90 were in Stage I, 109 in Stage II, 83 in Stage III, 27 in Stage IV and 93 in Stage V (recurrent).

Radical mastectomies were done in 202 instances. Major complications were partial sloughs of skin flaps in 34 cases and edema of the arm (never severe enough to be disabling) in 26 cases. In 149 of these cases followed for five years or more after operation, regional recurrences were recorded as follows: in the skin 24 cases, in the axilla 14 cases, in the supraclavicular nodes 16 cases. In 375 cases, including those treated by radical mastectomy alone and with preoperative and postoperative irradiation as well as cases of recurrent cancer following operation elsewhere, the predominant sites of metastasis were the lungs, pelvis, and spine.

Summarizing their results under a policy of operating upon all Stage I and Stage II cases and giving postoperative irradiation when axillary metastases were present, the authors found that 64 per cent of 42 Stage I cases (1926-41) were arrested for five years. The recurrences early and late, were nearly half in the skin and nearly a tenth in the axilla which suggests that the criteria for staging were not followed rigidly enough and/or also that microscopic examination of the axillary nodes was not searching enough. Thirty-five Stage II cases were treated by radical mastectomy alone (1926-41). A third of these recurred within five years, another third were arrested, and the remainder went on to late recurrence. Among 21 Stage II and III cases treated before 1941 with preoperative irradiation, there were only 7 five year arrests (including 3 late simple mastectomies in cases initially well controlled by irradiation). Seventy-five Stage III cases yielded only 2

five year arrests (x-ray irradiation) but many of the patients lived for several years with disease but in far comfort.

On the basis of their study the authors have discontinued the use of preoperative and postoperative irradiation in operable breast cancer, but they continue to be enthusiastic for the use of x-ray in holding in curable breast cancer in check and relieving the patient of the miseries of the disease for months or years. The beneficent effect of x-rays in the treatment of skeletal metastases is considered outstanding.

MAURICE D. SACHS M.D.

Radiation Treatment of Localized Malignant Lymphoma. George W. Holmes and Milford D. Schulz. *New England J Med* 235 789-791 Nov 28 1946

Malignant lymphoma has been accepted as the designation of malignant tumors that are characterized by progressive enlargement of lymphoid tissue in various parts of the body. Pathological classification has been extensive and varied. Clinically the course is more or less rapidly fatal with an average duration of life of two to three years. Some patients have survived for six years or more after surgical removal of the tumor. Cure has been assumed to depend on the extent, the location and the pathological type of growth.

The records of 500 patients with malignant lymphoma treated by irradiation were reviewed and 15 cases meeting the following requirements were found—a single lesion at the time of treatment (which consisted primarily in irradiation), biopsy diagnosis, five year survival without disease. There were 5 males and 10 females in this group. The youngest patient was ten years old, the oldest fifty-eight years. Abdominal lesions were found in 4 cases (in the mesenteric lymph nodes and gastro-intestinal tract), the peripheral lymph nodes were involved in 5 cases, and the tonsils (2 cases), larynx, parotid gland, femur and skin in the others.

Histologically there were 2 stem-cell, 1 clasmato-

cytic, 6 lymphoblastic, 3 lymphocytic, and 1 Hodgkin's lymphoma, 1 Hodgkin's sarcoma, and 1 follicular lymphoma. The x-ray dosage was 1,000 r or less in 9 cases, between 1,000 r and 2,000 r in 4, and over 2,000 r in 2. Radium was administered in 1 case.

Location did not seem to influence the result. It is the accepted opinion that if the entire growth can be removed a cure will follow. Findings in this study confirm this, indicating that if adequate irradiation can be administered before spread occurs, the tumor will be controlled. The duration of life would seem to depend somewhat on the type of tumor, but the information gained in this study does not confirm this, possibly because of the small number of cases. Localization of a disease at the time of treatment is probably an essential factor in cure.

JOHN B. McANENY, M.D.

Therapy for Soft Tissue Sarcomas. An Experimental Study. M. E. Maun, F. C. Jewell, and W. F. Dunning. *Surg., Gynec. & Obst.* 83: 653-656, November 1946.

The authors have attempted to evaluate the relative merits of radiation and surgical therapy in the management of soft tissue sarcomas in rats. The sarcoma was in its 148th transplanted generation and the progression of tumor growth was thought to be 100 per cent predictable. Various plans of treatment were instituted and the results were carefully studied. All of the animals were studied for lymph node metastasis, lung metastasis, size of tumor, and survival period. All the untreated rats had lymph node and lung metastases. The results of the various forms of treatment as measured by survival time are as follows:

	Cures	Uncured Rats, Days Survived (Average)
Control or untreated rats	0	31
Local excision of tumor after 17 days	0	40
Local excision after 10 days' growth	0	40
Röntgen therapy 1,000 r to tumor after 10 days' growth	0	39
Extremity amputated after 7 days' growth	50%	63
Röntgen therapy 1,500 r locally after 7 days' growth	0	50
Amputation after 7 days plus 1,500 r to tumor site and node bearing area on 7th and 9th days	71%	61
Röntgen therapy (1,500 r) only to tumor and node bearing areas on the 7th, 9th, and 11th days	30%	67

Röntgen therapy employed in this study was localized over the tumor or lymph node areas with the following factors: 100 kv, 15 ma, 4 mm Al filter, and 25 cm target skin distance. The most effective therapy seems to be amputation plus röntgen therapy. It is noteworthy that röntgen therapy alone prolonged the rat's life ten days as did local excision, and the authors feel that this is equivalent to one year of a man's life. The study is an interesting one and lends support to the use of combined surgical and röntgen therapy. It is difficult to say how far one may apply these principles in the management of sarcomas in man.

JAMES C. KATTERJOHN, M.D.

Treatment of Residual Lymphoid Tissue in the Nasopharynx by Radium. Leshe N. Gay. *J. Allergy* 17: 348-351, November 1946.

This paper is part of a Symposium on Infectious Asthma. The author discusses the results obtained by Crowe and his associates with the application of radium in deafness due to excessive lymphoid tissue. The relation of infected tonsils and infected adenoids to bronchial asthma has long been recognized, and it was observed in Crowe's series that many of the children who were deaf for the higher tones also had bronchial asthma. Many of these children were allergic to the usual inhalants but had failed to respond either to desensitization or to removal of the allergen. They had recurring colds associated with asthmatic attacks, and numerous islands of infected lymphoid tissue were present in the nasopharynx. Following irradiation, the attacks diminished in severity and frequency and in some cases ceased to occur. This beneficial effect may have been due to reduction in secretion, to decrease in the absorption of allergic substances by nasal and nasopharyngeal tissue, or to removal of the nasopharyngeal "culture tube" in which sensitizing bacteria thrive.

The author believes that a child who has frequent winter colds and an associated asthmatic bronchitis derives dramatic relief from a properly spaced course of radium therapy. It is wise to complete the treatment during the summer, for then respiratory infections are not so prevalent and treatment is less likely to be interrupted. A child who is sensitive to some allergen may get disappointing results from the usual desensitization treatment because of the secondary infection in the residual lymph nodes. In this group, irradiation is also of great assistance. In conjunction with specific desensitization therapy, irradiation has completely relieved many of these patients of their disturbing symptoms.

[For a description of the radium applicator and the technic of treatment, the reader is referred to abstracts in *Radiology* 44: 318, 1945; 47: 208, 1946.]

Evaluation of the Beta and Gamma Radiation Due to Extended Linear Sources of Radium. Robley D. Evans. *J. Indust. Hyg. & Toxicol.* 28: 243-256, November 1946.

The author's summary covers the material of this paper so adequately that it is quoted in full.

The beta and gamma radiation from extended linear sources of radium contained in a narrow radium gold foil covered by 0.3 micron of gold and 1.0 micron of nickel, have been measured and the results correlated with theory. At distances of a few feet from the active surface, the ionization due to beta rays is about 100 times the ionization due to gamma rays.

The proposed maximum permissible dosage level for beta radiation of 125 mrep [milli-roentgen equivalent-physical] per hour is found at distances of the order of 18 to 33 inches from unshielded sources of various lengths each containing 25 micrograms of radium per linear inch. Isodose curves are given for both beta and gamma radiation.

All the beta radiation can be absorbed by shields of 1/16 inch lead or 1/8 inch iron or 3/4 inch wood. Such shielding so arranged as to also prevent beta rays from being scattered towards the operators is desirable in industrial installations. If shielding is not feasible in particular installations, magnetic fields of the order of 2,000 gauss may be used to obtain about a ten fold reduction in the beta ray intensity.

If beta rays are excluded by shields, the residual gamma radiation equals the maximum permissible level of 12.5 mr per hour at distances of the order of 5 to 9 inches from sources of various lengths each containing 25 micrograms of radium per inch.

The alpha radiation is confined to a local region within about 3 inches from the radium source and accounts for the major portion of the effectiveness of such

sources in preventing the accumulation of static electricity in various industrial operations. When radium is used as the parent radioactive substance of the alpha radiation, the unwanted emission of beta and gamma rays is unavoidable. Consideration might well be given to the commercial development of alpha ray sources which emit little or no beta or gamma rays such as plutonium, protactinium, or polonium.

EFFECTS OF RADIATION

Effect of Irradiation on the Coagulation Time of the Blood in Normal Individuals Vincenzo Masini *Radiologia (Rome)* 2: 393-403 1945

The author reports the effect of 200 r administered over the spleen, liver, lower abdomen or buttocks of normal individuals upon the coagulation time of the blood. As compared with the coagulation time taken before irradiation, such treatment produces a decrease in the coagulation time with little variation in the fibrinogen and in the platelets.

CESARE GIANTURCO, M D

Protective Action of Desoxycorticosterone Acetate Against X-Ray-Induced Liver Changes Friedrich Elinger *Science* 104: 502-503 Nov 29, 1946

In view of his studies on liver changes incident to irradiation (*Radiology* 44: 241 1945) and the accumulated evidence that the symptoms of radiation sickness are attributable to histamine-like substances if not to histamine itself, the author conducted experiments to evaluate the protective action of desoxycorticosterone in irradiated mice. His studies revealed a marked reduction in the amount of sudanophilic fat in irradiated animals treated with desoxycorticosterone as compared with the untreated irradiated group. No striking difference in the radiation effects on the bone marrow or spleen was noted. Desoxycorticosterone was also found to have some protective action against the lethal effects of irradiation.

SYDNEY F THOMAS, M D

Action of Roentgen Rays on the Enzyme Catalase Arne Forssberg *Acta radiol* 27: 281-293, May 6 1946

The mode of action of roentgen rays on living organisms is discussed and the variation in sensitivity of the cells of different organs, tissues and species is noted in relation to the conditions under which radiation is administered. To study the problem of whether the action of radiation is direct 'the hit theory' or indirect a radiochemical action the author has investigated the effect upon the enzyme catalase, using a solution of the purified crystalline substance. By varying the catalase concentration of the solution the intensity of irradiation and the gas concentration of the solution results were obtained which indicate a complicated interaction of the irradiation products formed in the solvent with the enzyme as well as some direct action upon the enzyme molecules. Results obtained when the enzyme solution was frozen seem to indicate that the reac-

tion is predominantly in the immediate vicinity of the enzyme molecule.

ELIZABETH A CLARK, M D

Influence of Roentgen Rays on Isolated Cell Nuclei Hans van Euler and L Hahn *Acta radiol* 27: 269-280 May 6, 1946

Cell nuclei isolated from fresh calf thymus were irradiated with 25,000 r and 65,000 r to study the possible physiological change. Estimations of the phosphorus, nitrogen, desoxyribonucleic acid and histone content were made to determine the effect upon chemical properties. Viscosity measurements indicating the degree of polymerization, dialysis determinations for the molecular size of the proteins and an adsorption analysis to determine the ratio of dissociable and dissociated nucleoprotein molecules to the total protein were carried out in a study of the effect upon the physical properties. In none of the determinations was there significant difference between the irradiated nuclei and the control preparation. The author stresses however, that these results do not indicate biological inactivity of the cell nuclei.

ELIZABETH A CLARK, M D

Essential Safeguards in Production and Use of Atomic Energy John E Wirth *Occup Med* 2: 428-438 November 1946 *Atomic Energy in Industry and Physical Sciences* Samuel K Allison *Ibid* pp 439-446 *Physiologic Effects of Nuclear Energy* Shields Warren *Ibid* pp 447-451

The three papers listed above constitute a symposium on Atomic Energy in Industry and Medicine, presented at the Seventh Annual Congress on Industrial Health Boston 1946. The titles indicate the scope of the papers. Each emphasizes the importance of protection. According to Wirth essential safeguards in the production and use of atomic energy must be directed toward the working area and the surrounding community. They must encompass (1) personnel by education and organization (2) monitoring by the personnel and by a separate health physics unit stressing personnel monitoring, area surveys, research and developments (3) equipment such as personnel monitoring and area survey instruments, barriers, ventilation, protective clothing, techniques and handling devices (4) well trained laboratory personnel and special tests for analyzing human excreta for chemically and radioactively toxic elements. For details the original papers should be consulted.

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The Role of the Radiologist in the Management of Patients with Intestinal Obstruction, with Special Reference to the Use of the Miller-Abbott Tube¹

ELLIS C OSGOOD, M.D

Los Angeles, Calif.

THE PURPOSE OF the present study is to evaluate the role of the x-ray examination in the management of patients with intestinal obstruction. In recent years the radiologist's opportunity in this field has been extended by the introduction and increasing use of the Miller-Abbott tube. It is therefore proposed to consider in some detail the use of this tube, with particular reference to the radiological examination. Brief reference will also be made to the over-all improvement in the operative management as a result of the introduction of this surgical adjunct, and pertinent figures will be cited from a series of cases of small intestinal obstruction treated in the Hospital of the University of Pennsylvania over a five-year period.

With the onset of intestinal obstruction, many physiological changes ensue. A thorough understanding of these changes and their variation with the location, degree, duration, and nature of the occlusion are essential if the radiologist is to have a thorough understanding of the surgical problem and thus contribute to its solution. This phase of the subject has been amply covered by Wangenstein (41) and space need not be given it here. The clinical

features are likewise well known, and a brief summary of these will suffice.

Except in high obstruction, intestinal colic is the prime manifestation of intestinal occlusion, though in late cases bowel activity may be so reduced that clear-cut colic is recognized with difficulty. Distention invariably results if the obstruction is untreated. It may not, however, be clinically evident in early cases, and it is in the demonstration of its presence at this stage that the x-ray is of particular value. Vomiting is a prompt and persistent symptom of high obstruction and appears in most cases of small intestinal occlusion. It may be entirely absent in closed-loop obstructions of the colon or may be infrequent and of reflex origin. Persistent tenderness, fever, and leukocytosis are suggestive of strangulation. It is particularly important that this possibility be considered, since only if it can be ruled out is it justifiable to resort to suction drainage.

ROENTGEN DIAGNOSIS

While the clinical diagnosis of intestinal obstruction is often adequate, the roentgen examination offers valuable confirmatory evidence and in many cases is useful in de-

¹ From the Department of Radiology Hospital of the University of Pennsylvania, Philadelphia, Penna. Abridgement of a thesis submitted to the Faculty of the Graduate School of Medicine of the University of Pennsylvania toward the requirements for the degree of Doctor of Medical Science for graduate work in radiology. Presented, in abstract, at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec 1-6, 1946.

termining the location of the obstruction as well. Without the administration of barium, it is rarely possible to come to any conclusion as to the etiology, but it is never advisable to resort to the use of barium except by enema.

The roentgen examination is best begun with fluoroscopy of the chest or, if this is deemed too distressing to the patient, roentgenography in the upright position. This may disclose possible pulmonary disease, establishing the distention as of reflex origin rather than due to actual obstruction, or it may reveal conditions directly related to an obstructive lesion, as for example the presence of metastatic deposits. An anteroposterior roentgenogram of the abdomen, made with the aid of a Bucky diaphragm, with the patient supine, is most satisfactory for study of the outlines of the gas-filled intestinal loops (and of the undistended feces-filled loops as well). A comparable roentgenogram should also be made with the patient erect.

The interpretation of the roentgen examination should provide, if possible, the answers to the following questions: Is radiographically demonstrable gas² present within the intestinal tract and, if so, in what portion or portions? Are the distribution and amount pathologic or within normal limits? If distention is present, is it due to obstruction of the bowel lumen or to other, so-called reflex, causes?³ If distention is presumably due to obstruction, where is the obstruction? If the distention

is presumably reflex, is there anything in the roentgen examination to suggest the etiology?

The earliest roentgen sign of small bowel obstruction is the finding on the survey film of a small segment of distended gut.⁴ The outline is clean-cut, and the shape may resemble that of a hairpin, the so-called "hairpin loop" (39, Cases 1 and 2). Such an appearance may be seen as early as four hours after the onset of symptoms (23, 29, Case 1). The erect film in such a case may not show a fluid level in the distended loop. As the obstruction persists, the length of the distended segment increases, and the coils appear greater in diameter and lie transversely in the abdomen, one above the other, producing the "stepladder" pattern. At this time fluid levels are usually seen. In the later stages, the appearance is similar but more marked (Figs 1 to 6). In the earlier stages, the pattern of the distended segment resembles to some degree that of the barium-filled segment, the "feathery" pattern of the jejunum appearing as closely spaced, delicate, transverse striations, due to the valvulae conniventes. The more distal segments of the small intestine become less and less characteristic when distended, the transverse striations becoming less prominent, while the terminal portions of the ileum are, as described by Wangenstein, "characterless" (41, page 112, Fig 6). With high degrees of distention, the appearance of all levels becomes quite similar.

The position of the distended loop in the abdomen not only aids in differentiating small bowel from colon but also serves to differentiate between jejunum and ileum, loops of the former usually lie in the upper abdomen and to the left, while the latter is found more often in the lower mid abdomen.

Distention of the colon is easily recognized. The colon occupies a more or less fixed position around the periphery of the abdomen, so that when distended gut is

² It should be recognized that gas is always present in all portions of the intestinal tract. In some portions however it is so intimately mixed with the bowel contents that it is not recognizable on the roentgenogram. In the ensuing discussion the word *gas* will be used to denote that which is radiographically demonstrable.

³ Throughout the discussion the term *intestinal obstruction* (commonly used synonyms are mechanical obstruction and dynamic ileus) will be used to indicate the presence of a mechanical occlusion of the bowel lumen. In all other cases the term *reflex ileus* (commonly used synonyms are adynamic ileus, adynamic obstruction and paralytic ileus) will be used. This term implies a disturbance in the normal physiology of the intestinal tract resulting in stasis of the intestinal contents, distention and in some cases the collection of fluid, without obstruction of the bowel lumen. Reflex ileus may arise as the result of remote causes, such as disturbance of nervous control, or from actual pathologic changes in the bowel itself.

⁴ The word *distention* will be used to indicate the presence of a more than normal amount of gas in any segment of bowel, large or small.



Fig 1 The survey film demonstrates three gas filled loops of small intestine lying one above another. This is the appearance in early cases. The appearance in an earlier stage is illustrated in Fig 15. The latter is not a case of mechanical obstruction but the roentgen appearance is indistinguishable from that noted in this case. Fig 2 The appearance of distended loops of small bowel in another early case of obstruction. This is similar to the preceding case (Fig 1), but it is probable that more loops are distended. The increase in density between the filled loops probably representing other loops which are filled with fluid.

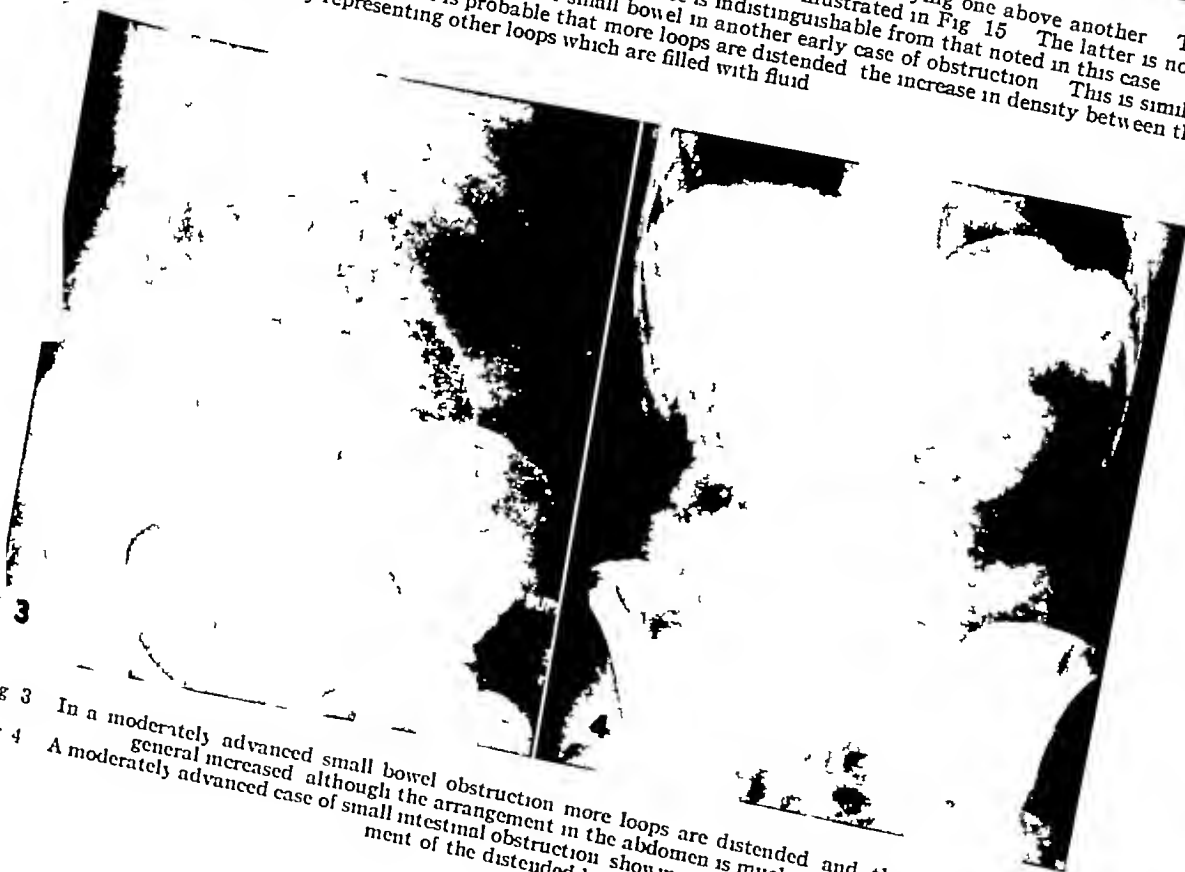


Fig 3 In a moderately advanced small bowel obstruction more loops are distended and their caliber is in general increased although the arrangement in the abdomen is much the same. Fig 4 A moderately advanced case of small intestinal obstruction showing somewhat less regularity in the placement of the distended loops.



Fig 5 The caliber and arrangement of the loops in a far advanced case of small intestinal obstruction are shown. The parallel arrangement still persists

Fig 6 The appearance of acutely distended small bowel after the administration of barium (An error Barium should never be given by mouth when bowel obstruction is suspected. Since the contents of the obstructed small bowel remain fluid the presence of barium does not increase the degree of the obstruction whereas in large bowel lesions, acute obstruction may be precipitated by the presence of drying masses of barium accumulating proximal to an incompletely obstructing lesion. However the presence of barium may complicate the surgical procedure and hence is undesirable.)

Note the gradual disappearance of the intrinsic bowel markings from jejunum to ileum. The ileum is rather devoid of characteristic markings (the structureless character as described by Wangenstein). Such loops may easily be confused with sigmoid loops and a barium enema is often necessary for positive differentiation.

Despite the acuteness of the obstruction, the lumen of the bowel was not completely occluded. A later film showed some barium in the colon.

seen occupying this position it is more easily identified as colon than are the more mobile loops of small bowel as jejunum or ileum. The haustral markings are usually visible—except in the lower descending colon and sigmoid, which, when distended, may very closely resemble loops of lower ileum—and are coarser and more widely spaced than the transverse lines of the upper small intestine. The presence of fecal material is also a great aid in identifying loops containing it as colon. The diameter of the distended colon is usually greater than that of a similarly distended loop of small intestine.

In the great majority of cases, obstruction of the colon is indicated by distention of the segments proximal to the site of the obstruction, with an absence of distention

distally and with no small bowel distention. The collection of gas between the obstruction and a competent ileocecal valve produces a so-called "closed-loop" obstruction, and it is the roentgen picture of this distended loop which is characteristic of large intestinal obstruction. Under such circumstances, it is the cecum which is usually the site of the greatest distention, even though the obstruction may be in the descending colon or sigmoid. The danger of perforation of the cecum in this type of case, as pointed out by Wangenstein, is real (40, 41, page 153). The exact location of the obstruction is often evident, being marked by the point at which the distention is seen to disappear abruptly, and beyond which no air, or only a normal amount of air, is present. At times, however, the distention

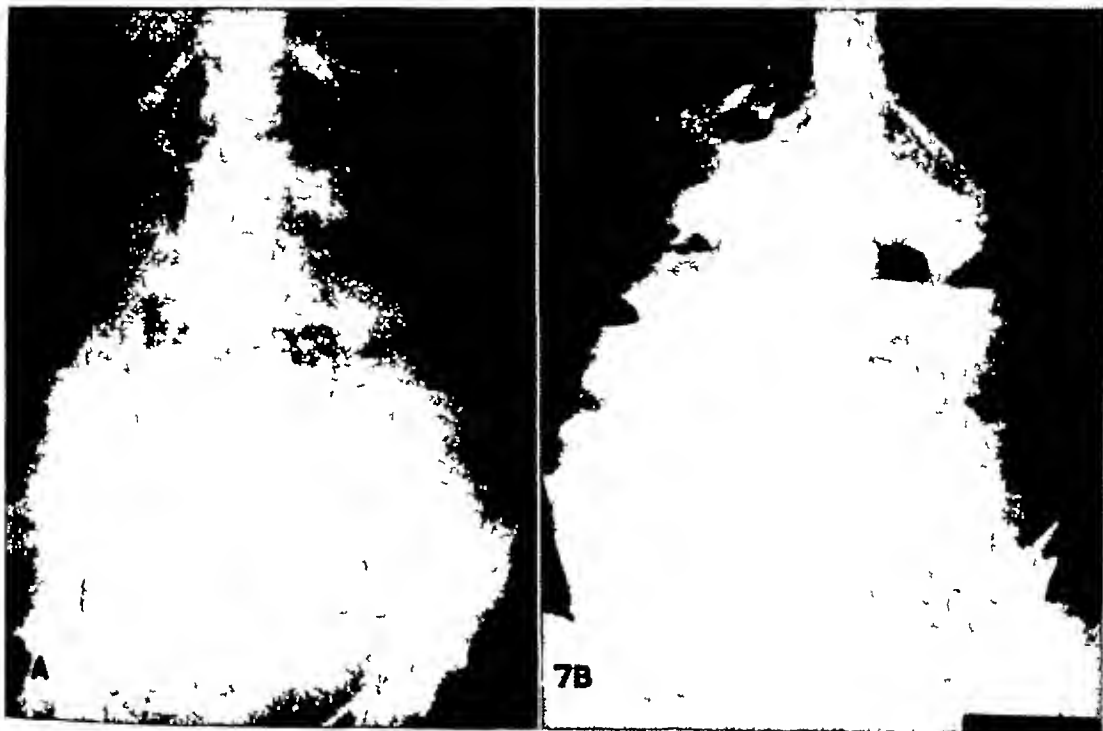


Fig 7 The supine film (A) of the abdomen shows only equivocal evidence of intestinal distention. The erect film (B) shows fully the extent of the small intestinal distention, with multiple fluid levels. If the supine film alone had been made, the examination might have been interpreted as negative.

may appear to be limited to the right side of the colon, very little gas being present in the descending colon and sigmoid, and yet examination by barium enema will reveal an obstruction in the sigmoid. In view of this fact, distention of the cecum and ascending colon alone is suggestive, and the possibility of a low obstruction should be investigated by barium enema. It is noteworthy that this distention of the cecum may be noted even in cases which are not of the closed-loop variety, namely, in cases in which there is reflux of gas into the ileum through an incompetent ileocecal valve (Figs 8 and 9). There is often considerable tenderness over a distended cecum, a circumstance which may lead to a suspicion of appendicitis rather than obstruction.

In occasional cases the distinction between the roentgen signs of small and large bowel obstruction is obscured by the location of the lesion—in the ileocecal region or just distal to the ileocecal valve—or by the presence of other than obstructive factors, commonly inflammatory.

Special circumstances apply to the diagnosis of obstruction in infants and children. The great majority of such cases are seen in infants and are congenital. The recognition of obstruction and its location is based on the absence of gas shadows in areas where they should normally be present.

The differential diagnosis between the manifestations of intestinal obstruction, as described above, and those of reflex disturbances producing intestinal distention is often difficult, and in many cases impossible, on the basis of the roentgen findings alone. In general, in cases of reflex distention, both the small and large bowel are involved, and the distention is less likely to be so uniform, with loops of both small and large intestine irregularly outlined and a conspicuous absence of a pattern suggesting continuity, which is the rule in organic obstruction (Fig 10).

Reflex ileus occurs in the presence of pulmonary infections, cholecystitis and cholelithiasis, renal stones and renal infections, in infections of the intestinal tract itself, in



Fig 8 Barium enema film showing a typical annular filling defect at the junction of the descending colon and sigmoid. This patient had had distention for several days and was vomiting. Note the extensive reflux distention of the small bowel. (In general, injection of barium into the colon should be carried out only to the extent necessary to demonstrate the lesion; larger amounts are unnecessary and may be deleterious.) Note the increased caliber of the cecum even though there is small intestinal reflux.

Fig 9 The survey film of the abdomen shows not only distention of the large bowel, but also extensive distention of the small bowel. At operation an obstructing carcinoma was found at the rectosigmoid junction. The distention of the small bowel was due to reflux through the ileocecal valve. Even with this "escape valve," note the high degree of distention of the cecum.

edema of the bowel (as in uremia and hypoproteinemia), and in embolism or thromboses of the bowel. Distention also accompanies peritoneal irritation, whether due to generalized acute peritonitis, chronic tuberculous peritonitis, or carcinomatosis. Retroperitoneal infections, *e g*, acute pancreatitis, and neoplasms, especially if involving the lymphatic structures, may also cause reflex ileus. Abdominal trauma and spinal cord lesions are common causes of ileus. The administration of drugs, especially morphine, may lead to distention. Conditions such as these should be looked for in any case of intestinal distention, particularly without typical intestinal colic, and in their presence a roentgen diagnosis of intestinal obstruction must be accepted with reservation until proved by barium enema or passage of the Miller-Abbott tube. Not infrequently a mechanical and a reflex ileus may coexist.

THE MILLER-ABBOTT TUBE

Advantages and Indications The introduction of the double-lumen, balloon-tipped tube by Miller and Abbott (33) in 1934 marked a significant advance in the study of small intestinal physiology, and in the diagnosis and treatment of selected varieties of intestinal disease. The therapeutic use of the tube was first suggested by Abbott and Johnston (5) for relief of the distention of intestinal obstruction, with the thought that suction applied at or just proximal to the obstruction should be more effective than that applied at a distance (Wangensteen duodenal suction drainage). That their premise was correct has been shown by subsequent events.

At the same time Abbott (1) pointed out that the passage of the tube to a point of arrest would provide an accurate localization of the obstruction, particularly if a

barium solution were injected into the tube and roentgen studies were made

Other advantages of the long tube soon became apparent. As the suction decompresses the bowel proximal to the obstruction, peristalsis returns (leading to further progression of the tube) and a normal segment of bowel is then available for the introduction of salt, fluids, and liquid nutrients. That portion of the nutrient fluid not absorbed may be removed. An intake and output record may be kept of the fluid given by mouth and that removed by drainage, and is a great aid in managing the electrolyte balance.

The opportunity to obviate the malicious effects of distention by decompression alone, without the hazard of surgical enterostomy, makes it possible for the surgeon to prepare the patient for operation over a longer period, and often converts an emergency into an elective procedure. The absence of a high degree of distention simplifies the surgical procedure. If the decompression is incomplete, as in cases of multiple obstructions, the tube may often be manipulated, at operation, past successive obstructions. With suction applied, each segment of obstructed gut may thus be decompressed without resort to direct aspiration. Following operation, the continued presence of the tube prevents distention and protects the suture line. Convalescence, therefore, is smooth, and complications, particularly new obstructions due to adhesions, are uncommon.

In general, the use of the Miller-Abbott tube is indicated in situations where the previously described advantages are desired. Distention, whether secondary to mechanical obstruction or of reflex origin, is relieved by decompression through the Miller-Abbott tube. In cases of mechanical obstruction the tube may be considered as a useful adjunct. It has proved in reflux ileus to be a therapeutic end in itself, since in such cases surgical enterostomy is generally conceded to be valueless, and sole reliance must be placed on non-surgical decompression. In such situations, the results have been truly brilliant.



Fig 10 The usual appearance of a paralytic or reflex ileus, in this case postoperative. The distention is scattered irregularly throughout large and small bowel, and the loops of bowel are not greatly increased in diameter. Much greater distention may be present in more severe cases.

In surgical procedures involving resection of the large bowel, the prophylactic introduction of the tube has proved of value. The reefing of the small bowel on the tube decreases the volume of the abdominal contents, making operation easier (31). The presence of the tube after operation, as mentioned above, prevents distention, protects the suture line, and leads to a smooth convalescence (14). Ravdin and Abbott (36) report the use of the Miller-Abbott tube in 26 such cases with one death, thirty hours after operation, as a result of coronary occlusion. Whipple (44), in reporting his experience with resections of the large bowel, both right and left, during 1938-40, without the use of the Miller-Abbott tube, records a mortality of 18.4 per cent of 76 cases, while in a group of 36 similar cases in which the Miller-Abbott tube was used there was only one death, a mortality of 2.8 per cent.

Contraindications There are few contraindications to the use of the Miller-Abbott



Fig 11 Barium administered in error in a patient with atypical abdominal symptoms in whom the presence of obstruction was not anticipated. The obstruction was chronic and at operation was found to be due to scarring secondary to a chronic ulcer at the site of ectopic gastric mucosa. Note the difference in the intestinal markings as compared with Figure 6. This change is due to the chronicity of the obstruction. The entire bowel proximal to the obstruction was several times its normal thickness and did not collapse when decompressed.

tube. It must not be used in persons known to have or suspected of having strangulation or gangrene of the bowel if operation is thus delayed. Its prophylactic advantages warrant its passage postoperatively, however. Since external hernias are readily approached, and since some contain strangulated loops, the use of the Miller-Abbott tube in such cases is contraindicated.⁵ The tube should not be used in obstructions of the large bowel. In these cases there is an increase in tonus of the terminal ileum which makes uncertain and delays entry of the tip into the cecum, and the cecal contents are ordinarily too grumous for aspiration through the tube.

⁵ Gatch and Montgomery (12) have recently described a method of treating strangulated external hernias which involves the use of the Miller-Abbott tube. The effectiveness of this method remains to be evaluated.

If there is reflux distention of the small bowel due to an incompetent ileocecal valve, decompression of the small bowel may be advantageous during the period in which the patient is being prepared for operation.

Complications. Few complications attend the use of the Miller-Abbott tube. Irritation of the upper respiratory passages may result, as from any indwelling nasal tube. Laryngeal damage has been reported in a number of instances (34, 42, 18, 22). Esophageal complications, particularly in patients with varices, have been recorded (19, 45, 16). Complications resulting from excessive coiling of the tube and from inability to deflate the balloon have been described (15, 37, 45, 20). In a case studied in this series (Case 9) a reverse intussusception was produced as the tube was withdrawn.

Technic. The successful use of the Miller-Abbott tube requires a detailed knowledge of the technic of its passage and care as established by past experience. The standard double-lumen tube arranged for suction distal to and proximal to a single balloon is most generally useful for routine diagnosis and therapy. This tube has an over-all diameter of 6 mm (18F), with walls approximately 1 mm in thickness. The lumina are unequal in size, the larger representing the suction side. The smaller lumen terminates just proximal to the metal tip and contains several small holes through which air may be injected into the balloon. The latter, made of thin rubber (condom or finger cot), is attached between the metal tip and the most distal suction aperture by means of silk thread. The proximal end of the tube is a metal Y-fitting, one side, marked "suction," connects with the suction side of the tube, the other, unmarked, with the balloon side. Modifications are available for purposes of special physiological investigation (7, 6, 2, 1, 21, 43, 3). The construction of a suitable tube using two tubes fastened together has also been described (2, 1, 35, 19). Johnston (19) favors the use of a No 16 or 18F Jutte tube, which is stiffer than the Miller-

THE USE OF THE MILLER-ABBOTT TUBE

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Abbott tube, to which is attached a small tube carrying the balloon

The tube to be used should be in good condition. A tube which has become soft and limp as a result of improper cleansing and sterilization is difficult to manage. The tightness of all connections between tube and fittings and the patency of the lumina should be assured. A balloon of proper size should be attached, curl the tip of the balloon will, when inflated, curl the tip of the tube, one which is too large will obstruct by overlapping the suction tip. The tube should not be tied so tightly as to bind the ends of the balloon to the lumina. After attachment, the balloon should be inflated and tested under water for leaks, and the suction side should be retested for patency. The ability to deflate the balloon should then be tested.

After thorough lubrication of the tip and preliminary local anesthesia of the esopharynx if desired, although this is rarely necessary, the tube may be passed through the larger nostril, into the esophagus, and thence into the stomach.

We prefer, at this point, to remove the patient to a fluoroscopic table. (If any delay in preparations for passage of the tube is anticipated, the patient may, if desired, be placed on the fluoroscopic table as soon as the decision to intubate is reached. Administration of fluids by venoclysis or hypodermoclysis may then be instituted and may be continued without interruption until passage of the tube is completed.)

With the patient comfortably arranged on the table, the suction drainage apparatus should be connected to the suction side of the tube and suction started. At this point, if not previously arranged, fluid administration may be begun. When the stomach has been emptied, passage of the tube through the pylorus may be attempted. While it is not always possible, especially in obstructions of some duration, to deflate the stomach completely (apparently because of continued reflux from below) this should be attempted. It is much easier to manipulate the tube through the

pylorus of a collapsed stomach than through that of a distended stomach.

Under fluoroscopic guidance, the tube should be withdrawn until the tip is at the cardiac orifice (unless the position of the tube, with the tip in the pyloric antrum, is already satisfactory). The patient is then placed on his right side and the tube is advanced. With the patient in this position, the pylorus is dependent, and gravity will carry the tip of the tube into the pyloric region. An attempt should then be made to pass the tube slowly, inch by inch, directly through the pylorus, under fluoroscopic guidance. In many cases the tube may be seen to enter the duodenum and traverse the duodenal curve. If the tube will not pass, a few inches of slack should be left in the stomach, care being taken that the introduction of this additional amount does not curl the tip upward in the stomach and away from the pylorus, and the patient should be allowed to rest, still lying on the right side. During this time suction should be maintained.

If, after one-half to three-quarters of an hour, no progress has been made, suction should be discontinued and the patient allowed to drink a glass of warm water, which may stimulate peristalsis enough to carry the tip through the pylorus. (Instead of water, something for which the patient has an appetite may act as a more effective stimulant to peristalsis. A case has been reported in which, after a glass of beer, which the patient had been craving for days, the tube passed rapidly.)

If the tube still fails to pass, suction should be re-established and the patient allowed another rest period, still lying on the right side. At the end of this period a further attempt at passage through the pylorus should be made. (Occasionally other positions, such as the prone or erect, may be more favorable, and should be tried.) If this fails, further time must be allowed, during which the tube may pass, or, if the situation is such that urgent passage is required, the tube should be removed, fitted with a stylet, and reintroduced. (Abbott advises attempting to



Fig 12 Two loops of tube have prolapsed through the pylorus Too much tube should not be passed into the stomach

pass the tube first without the stylet, since the latter's effectiveness depends, to a great extent, on previous decompression of the stomach. If, however, previous gastric suction has been used, one might well take advantage of the opportunity to use the stylet immediately.)

Abbott (4) has described the use of a wire stylet to stiffen the tube. His directions for its use are as follows

"Pierce the wall of the aspirating lumen of the tube at the 50 cm (2 feet) mark with a length of 0.4 mm (0.106 inch) diameter specially straightened, stainless steel vom Hofe leader wire and advance the tip of the wire to a point 2.5 cm (1 inch) above the most proximal aspirating hole in the tube. Bend a loop in the other end of the wire so that tip cannot advance distally. The terminal 15 cm (6 inches) of tube will then contain no wire. Pass the tube in the usual manner. With a temporary adhesive tape patch over the point at which the stylet pierces the tube wall, inject 300 c.c. of air into the stomach and advance the tube until it lies along the greater curvature. Hold the tube at the patient's nose to prevent its slipping out, and apply suction to remove the air. The stomach contracts, squeezing the tip of the tube ahead. The antral spasm, with concentric contraction, prevents the terminal 15 cm from coiling and

the stylet prevents coiling of the tube proximal to the antrum, where the stomach is more flaccid. Draw back the tip of the stylet from the pylorus and, by steady gentle pressure on the tube at the nose, advance the tip into the duodenum. Withdraw the stylet, and patch hole with thin rubber."

Unless the stomach is well collapsed, 2 feet of wire will often be found insufficient to reach the antrum. Hence it is wise to consider introducing the stylet 4 rather than 2 feet above the tip. In fact, if it is desired to avoid puncturing a hole in the active portion of the tube (patching is not always satisfactory), the wire may be introduced at the extreme proximal end. Presumably the use of an L- instead of a Y fitting, with the long arm of the L continuous with the suction side, would enable one to introduce the stylet the full length of the tube, with no puncturing of the walls necessary.

It is possible, furthermore, by the use of a longer stylet to extend the tip of the wire past the suction holes until it rests in the region of the balloon, or it may be passed along until the tip of the wire rests within the metal tip itself. If this technic is to be attempted, it is wise to slightly enlarge and blunt the end of the stylet by soldering, so that any accidental protrusion through the suction holes, or through the tube itself, would be less likely to damage the bowel wall. The increased stiffness of the tube makes considerable care necessary in introducing it through the nose and pharynx, but passage can be attained without undue trauma.

With the stylet extending to the tip of the tube, passage through the pylorus is sometimes attained with greater speed and facility than with any other method. If this method is used, the stylet is allowed to remain in place until the balloon has passed into the duodenum. The balloon is then inflated and, under constant fluoroscopic guidance, the stylet is removed. If the stylet cannot be withdrawn easily—it usually can be, particularly if it and the suction side of the tube have been lubricated previously with a thin mineral oil—the tube may have to be withdrawn into

the stomach and the stylet removed. In such cases, with the exact direction of the pylorus having been located, the tube can usually be repassed into the duodenum without the stylet. It is considered unwise to allow the tube to progress into the small intestine with the stylet in place (this could be possible only in instances in which the wire had been passed the entire length of the tube)



Fig 13 Prolapse of a loop of tube through the pylorus, through which the tip of the tube has already passed

After the balloon has reached the descending duodenum, 20 c c of air are injected into the balloon side of the tube. As the air is injected, the balloon should be observed fluoroscopically to make sure that it inflates. If the tip of the tube does not progress as the balloon is inflated, but regurgitates, the air should be withdrawn immediately and the tube be passed farther along the duodenum before the balloon is again inflated. More than 20 c c of air are unnecessary and possibly dangerous.

When the balloon has been inflated, the tubing leading from the balloon side is clamped with a hemostat and the handle of the latter bound with adhesive tape so that



Fig 14 Film showing an entire Miller Abbott tube in the stomach. A knot was present, which made it difficult to withdraw the excess. In the supine position, only a foot or so could be withdrawn. At this point the knot and an entangled loop were drawn into the esophagus. In the prone position, the loops disengaged themselves to the extent that all the excess down to the knot, which was about 8 inches proximal to the tip of the tube, could be removed. A slight excess of tube was left in the stomach overnight. Peristaltic activity untied the knot.

it cannot slip or be removed accidentally. It is well to mark the adhesive "Do not remove."

The patient may then be removed to bed, where the suction is re-established and fluid administration is resumed, if it has been discontinued during transfer from fluoroscopic table to bed.

The great difficulty sometimes experienced in getting the tube through the pylorus has led, in some quarters, to a lack of confidence in the usefulness of the tube. Much of the delay in the past has been due to failure to use frequent fluoroscopic or radiographic check-ups. If the tip of the tube is presumed to be at the pylorus, but actually is not, no amount of waiting will accomplish its passage. As more and more tube is introduced, loops form in the stomach, one of which may pass through the pylorus (Figs 12 and 13), or the tube

may even become knotted (Fig 14) In the latter event, Abbott has shown that provision of plenty of slack will enable the activity of the stomach to untie the knot If the tip of the tube is believed to be in the duodenum, but actually is not, and the balloon is fully inflated, passage will certainly not be achieved Abbott (1) originally described a syringe method of determining whether the tip had passed through the pylorus, but this test has not always been dependable (20)

Many other suggestions to aid in getting the tube through the pylorus have been offered, most of which have not enjoyed a very wide usefulness (32, 9, 38, 8, 41, page 156, 27)

The use of mercury in the balloon of the Miller-Abbott tube (41, page 164, 13) has been widely adopted and has been so effective that it has replaced, to a great extent, the use of the wire stylet. My own experience with this method has been quite satisfactory Two or 3 cc of metallic mercury are injected into the balloon (this amount is as effective as the larger amounts originally recommended by Harris) The patient is then turned on the right side and in favorable cases gravity will promptly carry the tip of the tube into the duodenum Although Harris states that in most instances the tube will progress well without air in the balloon, in my experience passage has been more rapid when air was injected into the balloon as usual Since mercury is chemically inert, no harmful effects are to be expected if the mercury should escape into the intestinal tract⁶ The tube is removed as usual with the mercury still in the balloon

⁶Mercury should not be used in the lumen of the Miller-Abbott tube with the assumption that if the balloon should break and mercury escape into the intestinal tract, no harmful effects would occur While no reports of such a harmful result have as yet been published, proof of the lack of toxicity under these conditions has not been established Leon Lewis (personal communication), who has had considerable experience with the toxicology of metallic mercury says 'The sort of emulsion which might form in the intestinal tract if the metal could not readily escape would I am sure render it absorbable and toxic Miller (personal communication), on the basis of the literature on the toxicity of mercury, feels that its escape into the intestinal tract is a definite hazard and advises against its use.

Most important of all to success in the use of the tube are experience, persistence, patience, and the use of fluoroscopic control In the earlier work with the Miller Abbott tube, many were reluctant to subject the patient to a number of hours on a fluoroscopic table, but as experience was gained, it became apparent that the hours lost while the tube was unknowingly curled in the fundus were more dangerous (The use of fluoroscopic guidance warrants a word of caution, especially if many observations have to be made Each period of exposure should be only as long as necessary, and adequate precautions should be taken to protect both patient and fluoroscopist from excessive exposure If the fluoroscopic examinations are made by one accustomed to the use of x-ray equipment, preferably the radiologist, the technique may be so planned that any patient may have all the examinations necessary without danger of over-exposure)

The value of experience is demonstrated by the success of Abbott, who personally passed most of the tubes used in the University of Pennsylvania Hospital, and of Johnston (19), who worked with Dr Abbott in the early years and in whose clinic in subsequent years 500 intubations were attempted with only 6 failures Comparable results have doubtless been obtained elsewhere by those with special experience and organization Close supervision over and personal responsibility for the passage of the Miller-Abbott tube are important if success is to be attained Bennett (8) says

"An individual who is familiar with the various methods of intubation must take the full responsibility and must be prepared to spend the time necessary for the procedure and for close observation of the patient Too often the surgeon who may be familiar with the principles but not the practice of intubation, is satisfied with the half hearted, inefficient attempts of the inexperienced members of the house staff Inexperience predicts a high percentage of failures invites complications and is responsible for the disregard which some physicians hold for intubation

The successful progress of the tube through the small intestine depends on the

maintenance of adequate suction and on continued inflation of the balloon. The correct operation of the suction apparatus must be checked frequently, and the suction side of the tube irrigated frequently in order to make sure of its patency. An accurate record should be kept of the amount of drainage, since this represents fluid lost to the patient which must be replaced, together with the chlorides contained therein. If replacement fluids are administered orally, these should be given with the necessary amount of salt. Foods given orally should be those which will leave only such residue as can be removed by suction if necessary and which cannot block the tube.

The balloon should be tested frequently for leaks by comparing the amount of air which can be withdrawn with the amount injected when the balloon was last inflated. Care should be taken that no more than 20 cc of air are injected, and that the nursing staff, while caring for the suction apparatus, does not in error deflate the balloon by loosening or removing the clamp on the balloon side. Occasionally, confusing the two sides, the nursing staff may clamp the suction side and attach the suction apparatus to the balloon, or even inject fluid into it. It is preferable to assign to the care of these patients a nurse who has been specially trained for this work.

During the period that the tube is progressing, the patient should be made as comfortable as possible. Special attention should be paid to mouth hygiene and to relief of the irritation of the nasopharynx. It is best, however, not to use mineral oil for the latter purpose, as suggested by some, because of the possibility of aspiration and subsequent lipoid pneumonia. The tube should be fastened to the cheek or forehead by a cloth tape (10) or a Montgomery type strap with rubber bands (17), as adhesive sticks to the rubber and makes further passage of the tube through the nose disagreeable.

If there is any doubt as to the ability or willingness of the patient to co-operate, and he cannot be watched *constantly*, re-

straints should be applied in such a way as to make it impossible for him to remove the tube. Such an accident not only requires repetition of perhaps hours of work, but may result in disaster if the tube is forcibly withdrawn with the balloon inflated.

The exact length of tubing which should be passed into the stomach during any period is difficult to determine except by frequent x-ray and fluoroscopic observation. In general, the tube should be passed into the stomach at approximately the same rate as it is leaving the stomach, so that not enough accumulates to prolapse or knot. The tube should not be fastened to the cheek unless a slight excess is present in the stomach, otherwise excessive reefing of intestine on the tube may occur.

In cases of simple mechanical obstruction, the tip of the tube usually moves quite rapidly down the small intestine and may be in the terminal ileum, if the obstruction is not higher, in twelve to thirty-six hours or even less. In cases of reflex or paralytic ileus, however, the progress of the tube is much slower, several days being required for the tip to reach the cecum. In Leigh's experience (24), 21 days were required for the tube to traverse the length of the small bowel in cases of ileus due to operative trauma, while in cases with edema of the bowel, 62 days were required. In the latter group, progress became more rapid with the disappearance of the edema as a result of diuresis or otherwise. Since the small intestine, as it is decompressed and the tube is passed down, characteristically reefs itself upon the tube, the full length of the tube may not be required. Frequent fluoroscopic or radiographic checks are necessary to make sure that there is not enough slack in the stomach to allow knotting or prolapse of an extra loop through the pylorus, either of which will stop the progress of the tube. The success of the decompression and the progress of the tip are also followed. It is important that roentgen checks be made not more infrequently than once every twenty-four hours so that, if the tube becomes arrested, a barium injection can be done to deter-

mine whether or not the point of obstruction has been reached

Some care should be exercised in removing the tube. This should be done slowly, over a period of several hours, after deflation of the balloon. It is wise to check the position of the tube, the possible presence of knots, and successful deflation of the balloon fluoroscopically before removal. If at any time during its withdrawal difficulty is encountered, a further check should be made before continuing.

Barium Injection The investigation by the injection of barium of cases of small intestinal obstruction in which the Miller-Abbott tube has been passed is not difficult. The injection studies are made at a time when the interval survey examinations have shown that the tip of the tube is no longer advancing. If the tip of the tube is arrested at the point of the obstruction, and there are no extraneous factors present, there should be at this time no intestinal distention. If distention is still present, and the suction is known to have been effective during the hours previous to the examination, then the tip of the tube has not yet reached the obstructed point (failure to progress may be due to reflex disturbance, deflation of balloon, etc.), the tip of the tube has reached one point of obstruction with one or more other obstructions lying distal to it, or the distention may be due to complicating factors, such as generalized peritonitis. The injection of barium, by showing whether or not obstruction is present, makes the evaluation of the findings much easier, as well as showing the location, and possibly the nature, of the obstruction if present. The value of this procedure in distinguishing between mechanical obstructions and reflex distention is indicated by Leigh and Diefendorf (25), who apparently have found the differentiation so difficult without it that they define paralytic obstructions as those in which mechanical obstructions are not demonstrated by intubation.

A suspension of one part of barium sulfate in four parts of water has been found satisfactory. While the shadow is not

dense, particularly if further dilution occurs as a result of the presence of fluid within the injected segment, a thicker solution is difficult to withdraw, and it is most important not to impair the usefulness of the tube by blocking it with a suspension so thick that it cannot easily be removed on completion of the examination. While the solution is being prepared, a survey film of the abdomen should be made for later orientation.

The barium suspension is injected into the suction side of the tube by attaching a syringe directly to the metal attachment. Sixty to 100 c c of suspension will usually suffice. If the injection is made with the balloon still inflated, fluoroscopy will show most of the barium collected in the segment proximal to the balloon. When the balloon is deflated, the barium will then pass by, although not always quickly, and not always without changing the patient's position. It should be remembered that a considerable part of the small intestine proximal to a point of obstruction is reeled upon the tube, so that when the balloon is deflated a variable amount will slip forward. As a result, the tip of the tube may change its position in the abdomen, and the point of obstruction will, in many cases, subsequently be found to be some distance from the tip.

Fluoroscopic observations are made with the aid of palpation and change in the patient's position as necessary to cause the barium to advance and to demonstrate the morphologic details to best advantage. Spot films are made as indicated. The configuration of the barium column varies in accordance with the conditions present. In some cases barium will be seen to advance only as the patient is rotated. This usually indicates the presence of a kink, such as occurs in many instances of adhesive obstruction. Sometimes barium will be seen to advance intermittently, its flow past the obstruction coinciding with a visible increase in the peristaltic activity and the occurrence of typical intestinal colic. In this type of case, while the obstruction is clinically complete, in that cessation of

suction or removal of the tube will result in immediate recurrence of intestinal colic, the fluoroscopic examination indicates that actually the lumen is not entirely occluded to fluids under the pressure of increased peristaltic waves. The incompleteness of the obstruction as observed under the above conditions has been previously noted by Leigh, Nelson and Swenson (26) and Abbott (1). Abbott (4) felt that as a distended bowel was decompressed there was an increase in its blood supply, with a consequent lessening of irritability and spasm and a return of peristalsis. It was to these factors that he attributed the fact that injection of barium after decompression often demonstrated an incomplete obstruction of the bowel lumen. It would seem, however, that the demonstration, in such a case, at the time of the injection, of fighting peristalsis accompanied by intestinal colic (and also immediate recurrence of distention if suction is discontinued) would indicate rather that the clinical signs and symptoms of acute obstruction may occur despite the fact that the bowel lumen is not entirely occluded. Further evidence in support of this thesis is noted in the occasional case in which, in error, a mouth meal is administered. While barium collects in the distended fluid-filled loops, films made at intervals do show some barium to have passed the point of obstruction.

In some cases, while barium is seen to pass a point of incomplete obstruction, distention of the loop immediately proximal to it will persist. This situation is usually encountered in cases in which the obstruction is of long standing, and at operation the wall of the bowel is found to be thickened and the lumen permanently widened (Fig 11).

The segment of bowel beyond the point of obstruction should be of normal caliber. If it is not, and particularly if fluid and gas are present, the possibility of a more distal obstruction should be considered. Under these circumstances, observations by films or fluoroscopy should be continued until the barium has had a chance to reach such

an obstruction. If the distance is great, however, it is likely that the barium will be so diluted as to lose its diagnostic value.

If no barium is seen to pass the point of obstruction at the first observation, further observations should be made at intervals. During this time, the suction apparatus should be disconnected, to test the patient's tolerance to the discontinuance of suction. When the examination has been completed, the barium which remains proximal to the obstruction should be removed by irrigation and suction.

The value of the barium injection lies primarily in the determination of the presence or absence of obstruction. In the exact determination of the nature of the obstruction the examination is not so valuable, although in many cases the demonstration of an incomplete obstruction with sharp angulation of the bowel at the point of occlusion is suggestive of adhesions. The nature of obstructions due to other causes is not always revealed.

The demonstration of the anatomical degree of obstruction does not always determine whether or not eventual operation will be required. Complete obstructions may not require operation if, during the course of continued decompression, the etiologic factors disappear, as may frequently occur. Obstructions demonstrated by intubation and injection to be incomplete may, on the other hand, be persistent and require operation, since discontinuance of decompression, even for a few hours, may lead to prompt recurrence of intestinal colic and distention.

Evaluation of Usefulness The past forty years have witnessed a significant drop in the mortality rate for patients with intestinal obstruction. Many factors have contributed to this decline. The earlier recognition of the presence of obstruction, due in great part to more frequent roentgen examination and greater experience with, and reliance on, the roentgen findings, has in many cases made the immediate operation a truly early one in so far as the duration of the obstruction is concerned. There is no disagreement with the belief that early

operation, if it could be carried out in every case, would be the greatest single factor in a successful outcome. McKittrick and Sarris (30), for example, had no deaths in 42 patients with acute mechanical obstruction of the small bowel operated upon within twenty-four hours of the onset of symptoms, while in 17 patients admitted within twenty-four hours of the onset of symptoms but not submitted to emergency operation the mortality was 29 per cent.

Improvements in operative technic have undoubtedly played a part in the reduction of mortality, but probably more important than this has been the improvement in the non-operative adjuncts to therapy which were instituted following the introduction of the newer concepts of the pathologic physiology. First among these was the appreciation of the necessity for correcting an abnormal fluid balance and maintaining a normal balance until such time as operation could be carried out and convalescence established. Later, the malicious effects of distention alone were recognized, and methods for intestinal suction developed. The correction of fluid balance and the relief of distention have enabled the surgeon to treat more successfully the case which, when first seen, is already beyond the stage when operation, no matter how immediate, could be considered early.

In selected cases the use of sulfonamides at the time of operation and postoperatively has also contributed to a decreasing mortality. The applicability of penicillin is now being studied.

While the value of the above factors is evidenced in a declining mortality rate, the degree to which each is responsible for the decline is obviously difficult to evaluate statistically. This is particularly so for the use of intestinal suction, and for any assessment of the value of the Miller-Abbott tube as compared with the simpler and older method of duodenal suction.

Statistics in the recent literature and from the Peter Bent Brigham Hospital were evaluated in 1942 by Blodgett (11). His study concerned simple mechanical obstructions of the large and small bowel.

In a group of 306 cases without complicating peritonitis in which suction was not used (suction implied actual presence of the suction tube in the jejunum) the mortality was 17.3 per cent, while in 151 cases in which suction was used the mortality was 7.9 per cent. In a group of cases complicated by peritonitis, there was a mortality of 73.1 per cent in 56 cases in which intestinal suction was not used, and a 25 per cent mortality in 52 similar cases treated by suction. These differences were calculated by Blodgett to be statistically significant.

Leigh and Diefendorf (25) treated 132 cases of non-inflammatory mechanical obstructions of the small bowel by surgery and the Miller-Abbott tube, performing 103 operations in this group. The mortality was 4.6 per cent. In a similar group of 94 cases complicated by peritonitis there were 70 cases in which the Miller-Abbott tube was passed into the small bowel, with a mortality of 15.7 per cent, and 24 cases in which the tube was not used or did not pass into the small bowel, with a mortality of 32.5 per cent.

Whipple (45) treated 311 cases of acute ileus (presumably including paralytic obstructions and those with peritonitis) by surgery and the Miller-Abbott tube, with a gross mortality of 13.5 per cent. In 248 cases successfully intubated, the mortality was 9.7 per cent, while in 33 cases in which the tube failed to pass, the mortality was 54 per cent.

McCleery (28) reported 101 cases of simple mechanical obstruction of the small bowel treated between 1935 and 1940, without reference to the use of suction drainage. There was a mortality of 21 per cent in this group.

McKittrick and Sarris (30) in 1940 reported a group of 136 cases of acute mechanical small bowel obstructions, 33 per cent of which were strangulated. The gross mortality was 20 per cent. The mortality of the non-strangulated cases was 3 per cent. The mechanical factor of distention at operation was said to be a factor in 30 per cent of the deaths in the

series No statistical data are given in reference to the use of the Miller-Abbott tube in these cases In 1941 McKittrick (29) reported 18 cases of simple small intestinal obstruction with no deaths "In two patients, both over 60 years of age, decompression by means of the Miller-Abbott tube was life-saving From a review of these cases it is quite likely that had early operation been instituted, death would probably have resulted in each case "

An analysis of cases of small intestinal obstruction seen in the Hospital of the University of Pennsylvania follows ⁷

UNIVERSITY OF PENNSYLVANIA CASES, 1939-43

Small Intestinal Obstruction, Non-Strangulated,
No External Herniae, No Generalized Peritonitis

Total obstructions	53
Total patients	49
Age	
Under 25	5
25 to 50	24
Over 50	20
Sex	
Male	18
Female	31
Duration before admission	
One day	6
One to five days	13
Over five days (including those with indefinite histories and chronic cases)	34
Total cases using Miller-Abbott tube	34
Successfully	29
Unsuccessfully	5
Hours required for Miller-Abbott tube to pass into duodenum	
Less than twenty four	25
Twenty-four to forty-eight	2
Forty-eight to sixty	2
Would not pass	3
Would not pass through gastro-enterostomy	2
Hours for Miller Abbott tube to pass to site of obstruction	1 to 4 days
Day of operation after Miller Abbott tube passed	1 to 7
Days Miller-Abbott tube in, in non-operated cases	1 to 5
Days Miller-Abbott tube in after operation	2 to 6

⁷ Thanks are due Drs E E Eliason and I S Ravdin for permission to study the records of patients treated on their services

Location of obstructions	
Duodenum	1
Jejunum	6
Ileum	35
Multiple or undetermined	11
Degree of obstruction	
Complete	28
Partial	25
Etiology of obstruction	
Kinking or constriction due to adhesions	35
Jejunal ulcer with stenosis	1
Peritoneal carcinoma	6
Internal hernia	2
One herniation of gastrojejunostomy through gastrocolic omentum, one herniation through hole in mesosigmoid	
Appendix	2
One abscess with adhesions, one case of postoperative adhesions (perforated appendix)	
Gallstone ileus	1
Carcinoma of pancreas	1
Tumor	3
One intussuscepting myxoangioma, one intussuscepting leiomyoma, one adenocarcinoma of ileum	
Regional ileitis with abscess and adhesions	1
Operations	
Lysis of adhesions	25
Ileocolostomy	2
Resection of small intestine	5
Enterointerostomy	2
Gastrojejunostomy	2
Ileostomy	4
Release of internal herniae	2
Jejunojejunostomy	1
Removal of gallstone	1
Exploratory only	4
Cases not operated (all adhesions)	
Miller-Abbott tube used	4
Miller-Abbott tube not used	1
Deaths in hospital	5
Four patients had peritoneal carcinomatosis, one died of pulmonary complications but with obstruction relieved	
One patient had regional ileitis with multiple localized abscesses and fistulae	
Deaths outside of hospital	2
Obstruction unrelieved by hospital treatment Both had peritoneal carcinomatosis	
Gross mortality	
By patients	14 3%
By cases	13 2%

Corrected mortality	
Excluding all deaths, since in each instance the obstruction was only an incident in an otherwise irremediable disease	
Roentgen diagnosis	
Survey films	30
Positive diagnosis (all correct)	20
Negative diagnosis (all incorrect)	5
Inconclusive	5
Gastro-intestinal series (all correct)	4
Injections of Miller-Abbott tube (all correct)	16
Complete obstruction demonstrated 3 times, incomplete 13 times	

PHILOSOPHY

It is apparent that the patient with intestinal obstruction has a much greater chance of survival today than even a decade ago. The mortality, however, is generally high, except in selected centers where special interest is taken in these cases and special organizations have been developed for their treatment. Under such circumstances, many patients in the advanced stages of obstruction may be cured, and the superiority of results in such centers is probably largely accounted for by this group. There is no doubt, however, that wherever medicine is practised good results may be expected without extraordinary skill or special equipment, provided an early diagnosis can be made and treatment instituted promptly thereafter. All series of statistics show that, regardless of fluid administration, blood transfusions, duodenal or Miller-Abbott intubation, or other procedures, the mortality is lowest in that group of patients operated upon within a few hours after the onset of symptoms, and a successful outcome may be anticipated in this group even though none of the non-surgical adjuncts is employed. It is possible, therefore, for the surgeon who sees such cases only infrequently to secure as good results as his colleague for whom intestinal obstruction holds a special interest, provided only that the patient is referred to him early.

The responsibility devolves upon the physician first consulted, be he general

0 0% practitioner, internist, or gynecologist, to consider whether or not his patient may have intestinal obstruction and to take appropriate steps to establish the diagnosis. It is at this point that the radiologist has his greatest opportunity to contribute to a successful outcome. The radiologist who has the proper clinical background may consider, with the referring physician, the symptoms and physical findings which are so necessary to the interpretation of the x-ray examination which is to follow.

In so far as the latter is concerned, an attempt has been made to emphasize the roentgen findings which may indicate obstruction in its earliest stages. While it is true that multiple distended loops of small intestine containing fluid levels often point to obstruction, this appearance is not in itself diagnostic and is certainly not indicative of the early stage at which diagnosis is optimally established. Furthermore, cases have been cited which show that such findings may not indicate obstruction at all, at least in the sense of mechanical blockage of the intestinal lumen. The importance of the latter concept lies in the fact that exactly the wrong method of treatment—intestinal intubation—may be elected on the basis of a mistaken diagnosis delaying operation, which should be done immediately. Such errors may usually be avoided if overconfident reliance is not placed upon the roentgen findings to the exclusion of the clinical observations and laboratory data. It is evident, therefore, that, despite the importance of the roentgen examination, an exactly correct objective diagnosis may not be given in all cases. Furthermore, under such conditions the radiologist, unless he is an astute clinician and in possession of all the facts, cannot take it upon himself to do more than confer with the surgeon as to the type of treatment to be elected. The latter responsibility must fall upon the surgeon.

Provided intestinal intubation is decided upon as a preoperative therapeutic adjunct, or, in cases involving the colon, for its postoperative effect, the radiologist

is in a position to participate in the actual treatment of the patient. An attempt has been made to point out the value of radiologic procedures in the passage of the tube, and for study of the intestinal tract after the tube is in place, and to describe those procedures in some detail in the hope that the radiologist, becoming more familiar with them, will be better able to participate.

The part the radiologist may play will vary from simple fluoroscopy to more or less complete responsibility for the passage of the tube and its care. In highly organized clinics where special personnel is available, a system of division of labor and responsibility will probably prevail, but good organization whatever its nature, will lead to good results. Successful use of the Miller-Abbott tube, as indicated above, requires that definite responsibility for its use must be accepted somewhere along the line, and it is our opinion that under many circumstances the radiologist may well volunteer to accept this responsibility. His possession of the necessary fluoroscopic and radiographic equipment, his more or less constant presence in the hospital, and the probable availability of time make it logical for him to do so. We feel that by so doing the radiologist has a great opportunity to perform an important service to the surgeon and his patient. We are convinced that under such a system, the patient may benefit from the use of a procedure which might otherwise be neglected or even fall into complete disrepute.

Diagnostic procedures performed by injection of barium through the Miller-Abbott tube have been described. Our experience has not established their indispensability, however. While the studies have demonstrated, again, the physical incompleteness of many small intestinal obstructions, they have not indicated to any significant extent the necessity for operation. In this respect the clinical observations as to whether or not there is a recurrence of intestinal colic and distention after discontinuance of suction have been more important.

CASE REPORTS

CASE 1 A B, a 30-year-old white male, had been operated on several times in another city, a resection of the bowel having been performed in stages. Following these operations, the patient had enjoyed good health until 8 P.M. on the evening of admission, when he was seized with sudden severe abdominal pain, colicky in character. He was admitted to the hospital four hours after the onset of symptoms, at which time he was suffering from intermittent crampy pains, accompanied by hyperactive peristaltic rushes. No distention was evident clinically. A survey examination of the abdomen showed a distended loop of small intestine, "hair-pin" in character, on the left side of the abdomen. The erect film showed no fluid level. A diagnosis of intestinal obstruction was made, and immediate operation was performed. The abdominal incision was made directly over the region occupied by the distended loop. A short segment of distended gut was found proximal to an annular constriction. A resection and anastomosis were done and the patient recovered without incident. The constricting lesion was pathologically an adenocarcinoma.

This case demonstrates the rapidity with which a roentgenologically demonstrable degree of distention may develop (four hours after the onset of symptoms), the value of the distended loop in locating the abdominal incision, and the importance of immediate operation.

CASE 2 (Fig 15) W B, a 42-year-old colored male, was admitted to the hospital at 7 P.M. on Jan. 9, 1941. Three hours earlier he had been injured by a falling board, which knocked him to the ground and struck him across the abdomen. On admission his temperature was normal and the blood pressure was 165/110. Examination of the chest showed an enlarged heart. There were moderate abdominal resistance and tenderness, such as might be expected from trauma to the abdominal wall. There was no abdominal pain or colic. The patient had a large right inguinal hernia with a large scrotal sac in which no intestine was present.

The blood count was normal. Fluoroscopic examination showed cardiac enlargement, hypertensive in type, and some restriction of motion of the left diaphragm. Radiographic examination of the abdomen showed a sharply localized area of small bowel distention in the right lower quadrant. No fluid level was noted in the erect film.

During the ensuing two days, the abdomen became more tender and distended, ascites was clinically evident, the temperature rose, and x-ray examination showed a progressive increase in the number and size of the distended loops of small intestine. Fluid levels appeared.



Fig 15 Case 2 Early distention in a case of traumatic enteritis



Fig 16 Case 3 Dilatation of loops due to interference with blood supply



Fig 17 Case 4 Constriction of small intestine by a single adhesive band

The admission diagnosis was traumatic enteritis, and expectant treatment was elected. After two days of increasing signs and symptoms, however,

operation was performed. The abdomen contained considerable serosanguineous fluid. A segment of the ileum was ecchymotic and contained bloody fluid. There was considerable plastic exudate on the serosal surface. The involved segment was considered viable, however, and resection was not performed. Recovery followed a stormy postoperative period.

The interesting feature of this case is the rapid appearance in the presence of non-obstructive ileus of a locally distended segment of small intestine, eventually with fluid levels, of a character which could not, from the roentgen appearance alone, be differentiated from a mechanical obstruction.

CASE 3 (Fig 16) G J, a 35 year old white male, was admitted with a history of abdominal pain for the past thirty-six hours. Intestinal colic was not present. There was generalized abdominal tenderness, most marked on the left side, where there was a suggestion of a palpable mass. The temperature was elevated, and there was a polymorphonuclear leukocytosis with a slight shift to the left.

The supine film of the abdomen showed multiple loops of distended small intestine. In the erect position multiple fluid levels were noted. The roentgen examination was compatible with intestinal obstruction of the mechanical type, but the clinical features were not in accord, unless a complicating lesion, such as strangulation, was also assumed.

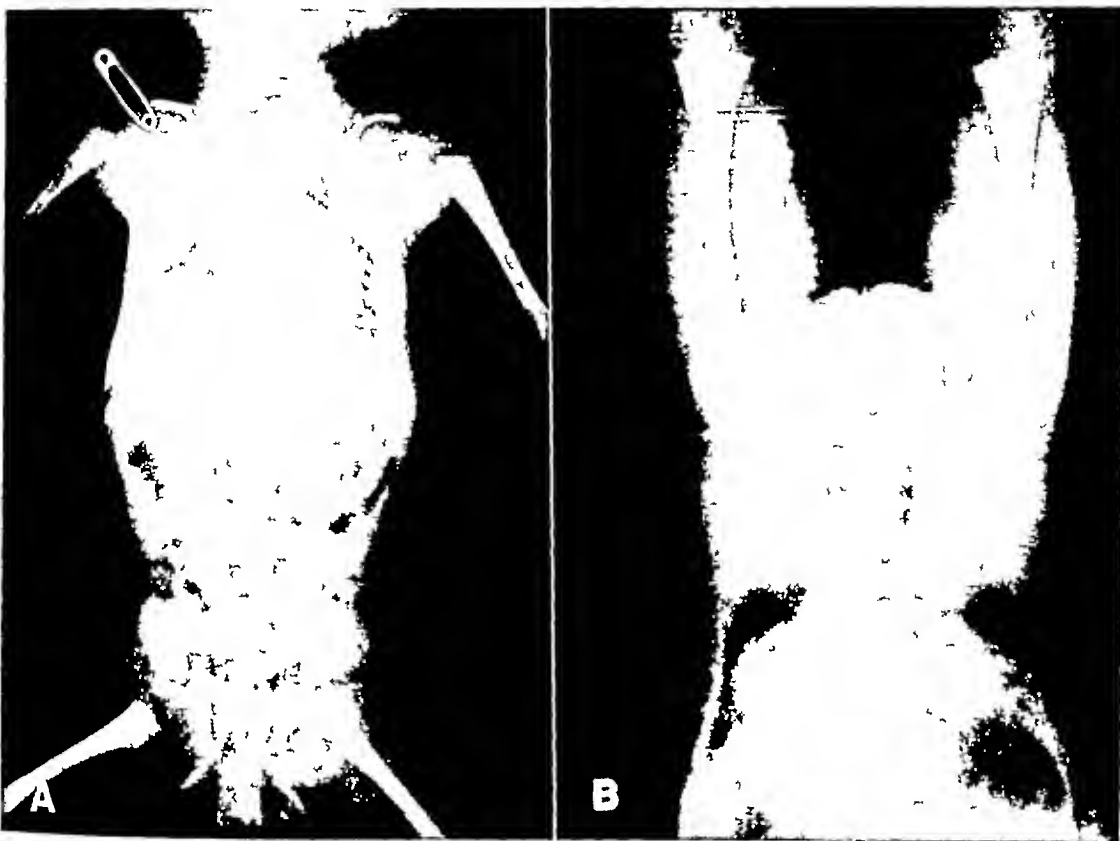


Fig 18 Case 5 Duodenal obstruction associated with rectal atresia in a four-day old infant A Supine film B Film made with patient inverted

At operation a mass was found on the left side of the abdomen. A major portion of the omentum had slipped through a fibrous band crossing its base (the origin of the band was not apparent) and had become twisted, incarcerated, and gangrenous. Multiple loops of small intestine had become loosely adherent to the gangrenous omentum. They were moderately dilated, and their walls were edematous and purple. There was fluid, not definitely bloody, in the intestinal lumen. The loops of intestine were readily separated from the mass by blunt dissection. When all were freed, there was no diminution in caliber and peristalsis did not return during the period of observation. However the intestine was considered viable. The omental mass was resected and the abdomen closed. A stormy postoperative course was expected, but convalescence was surprisingly uneventful.

It is apparent from this case that distention of the small intestine with multiple fluid levels is not of itself diagnostic of mechanical obstruction. The obstruction here was reflex in origin, since no block of the intestinal lumen was present.

CASE 4 (Fig 17) E G, a 74-year-old white female, had had a resection of the ascending colon, with ileocolostomy, two years previously for carcinoma. Except for constipation, she had been well until two days before admission, when crampy abdominal pain developed. There had been no bowel movement since that time. On admission, the abdomen was moderately distended and typical intestinal colic was present. There was no fever or leukocytosis, and no fecal impaction.

A supine film of the abdomen showed considerable air in the remaining colon, which, however, was not greatly increased in caliber, with multiple moderately distended loops of small bowel. (An erect film, unfortunately, was not made.)

A barium enema study was done in order to rule out the possibility of a second, possibly sigmoid, carcinoma. No abnormality of the colon could be demonstrated. Barium passed through the enterostomy stoma into the small bowel, which was distended with air and fluid. The exact site and nature of the obstruction could not be visualized. At operation the small intestine was found to be constricted just above the stoma by a single adhesive band. This was divided, and an uneventful recovery ensued.



Fig 19 Case 6 Obstruction due to malrotation in a two-day-old infant

In this case the obstruction of the small intestine, while sufficiently complete to result in intestinal colic and distention, was not complete enough to prevent air from passing into the colon. Apparently, therefore, in some cases, air may be present in the colon in considerable amounts in the face of a clinically acute small intestinal obstruction. Furthermore, clinically complete small intestinal obstruction may occur in the face of an incomplete obliteration of the intestinal lumen.

CASE 5 (Fig 18) B L, a 4-day old slightly premature infant, was born with an imperforate anus. During the first two days of life the distention which should have appeared as a result of the rectal obstruction did not develop, and gavage feedings were repeatedly vomited. A supine film of the abdomen showed far less air in the intestinal tract than normal. The stomach and proximal duodenum were greatly distended, indicating a duodenal obstruction which explains the absence of the expected distention which should have resulted had the rectal obstruction been present alone. A film in the inverted position showed the extent of the rectal atresia. (If operation is contemplated for repair of the anal defect the roentgen

examination should be made after the anal dimple has been marked with a small piece of lead, and a lateral view should be included, both views being made with the patient inverted.)

CASE 6 (Fig 19) B B, a 2 day old infant, vomited within a few minutes of completion of each feeding. A gavage tube was readily passed into the stomach.

An x-ray examination of the abdomen showed an abnormally small amount of air in the intestinal tract. The stomach was not greatly distended. A film made twenty-four hours later showed a marked distention of the stomach and proximal duodenum. In these cases the absence of air in the small and large bowel is more important than distention proximal to the obstruction, the latter may or may not be evident, depending on the time the examination is made. Operation showed an obstruction of the duodenum due to malrotation.

CASE 7 V Y, a 68-year-old white female, was admitted to the hospital complaining of abdominal pain and swelling. Her illness had begun two days earlier, with nausea and vomiting, but no pain. On the second day, severe diffuse abdominal pain appeared, which later in the day was limited to the lower abdomen. Chronic constipation, increasingly severe, had been present.

On examination dehydration was noted, with moderate abdominal distention. Tenderness was more or less diffuse. An occasional peristaltic tinkle was heard. Rectal examination was negative. The temperature was 99.4° , the white blood cell count was 10,030 cells per cu mm, with 77 per cent polymorphonuclears.

An x-ray examination of the abdomen showed a moderate distention of the large bowel as far down as the sigmoid. No small bowel distention was demonstrable. The findings were thought to be compatible with a low obstruction of the colon. Examination by barium enema showed a redundant sigmoid, in which lay a number of large fecal masses. Barium flowed through this area with great difficulty, but eventually the whole colon was filled, and no other abnormality except a moderate distention, was noted.

At operation, the colon was found to be distended. Several distended loops of small bowel were also present on the right side of the abdomen. Two large, hard fecal masses were obstructing the sigmoid. The appendix was perforated, and a localized pelvic peritonitis was present. The appendix was removed, a drain was placed in the pelvis, and the fecal masses were broken up. Recovery took place.

While the exact sequence of events in this last case is unknown, it is felt that the chronic obstruction produced by the fecal impaction, with subsequent distention of the cecum and appendix, may have led to the appendiceal rupture.

CASE 8 (Fig 20) W P, a 56-year-old colored male, was admitted to the hospital complaining of swelling of the abdomen and vomiting. For the past four months he had noticed a gradual increase in the size of his abdomen and increasing frequency of urination. On the evening of admission he experienced intermittent, generalized abdominal pain and began to vomit. Constipation had always been present, and although there was a bowel movement on the day of admission, the material passed was scanty.

The blood pressure was found to be 160/100, temperature 100°. The abdomen was greatly distended and somewhat tender throughout. Peristalsis was infrequent but, when it occurred, was high-pitched in type. A distended bladder was readily palpable. The rectal examination showed the prostate to be only slightly enlarged. No masses were felt. The catheterized urine showed many white cells. The blood count was normal. A survey examination of the abdomen showed an extensive distention of the colon, with little or no gas in the small intestine. The cecum was not as distended as the descending colon. No air was seen in the lower sigmoid or rectum. On the basis of the history, physical findings, and x-ray appearance, a diagnosis of low obstruction of the colon was made. After several hours of slow decompression of the bladder had failed to alter the situation, a cecostomy was performed for the relief of the large bowel distention. The patient improved rapidly. Catheter drainage of the bladder was continued, and the urinary infection responded well to sulfadiazine.

Several days after operation a barium enema examination revealed a locally spastic sigmoid, but no evidence of obstruction. The examination was repeated several days before the cecostomy was allowed to close and again revealed no organic lesion.

This case demonstrates the advisability of a preoperative barium enema in all cases in which a diagnosis of large bowel obstruction is made from the survey examination and shows how closely, under appropriate combinations of circumstances, a reflex ileus may resemble a mechanical obstruction.

CASE 9 L L, a young colored female, was admitted to the hospital July 30, 1943, with the signs and symptoms of an acute surgical abdomen. At operation, a ruptured tubal pregnancy was found. The tube and ovary were removed.

During the first postoperative week, there were some vomiting and moderate abdominal distention. The temperature was not elevated. Gas was being passed by rectum and peristalsis was present. By Aug 6 the distention had not decreased and, while it was felt to be reflex in origin, the possibility of adherent loops in the pelvis was considered. Ac-



Fig 20 Case 8 Distention of colon, simulating that seen in mechanical obstruction in a case of reflex ileus

cordingly, Miller-Abbott intubation was effected. During the next three days the tube progressed satisfactorily, and the distention was reduced. The tube was removed on Aug 11. X-ray examination the following day showed some residual small bowel distention, and vomiting reappeared. On Aug 13, the patient was seized with acute abdominal pain, tenderness and rigidity appeared, and the temperature rose to 101.8°, with a pulse of 100. Operation disclosed a perforated jejunal intussusception about 2 feet distal to the ligament of Treitz. The operating surgeon felt that the intussusception was in the reverse direction and that it had probably been produced as the Miller-Abbott tube had been withdrawn, even though the tube had been removed with all precautions thought necessary to prevent this theoretically possible complication.

Resection of the involved gut was carried out, and the patient recovered, although with a jejunal fistula. The latter was subsequently closed.

CASE 10 (Fig 21) L S, a 32-year-old white female, was admitted to the hospital complaining of severe abdominal pain. On examination the abdomen was moderately distended, with tenderness fairly well localized on the right side, somewhat above McBurney's point. The results of the rectal and pelvic examination were not available. Definite intestinal colic was not present, in fact, peristalsis was hypoactive. There was slight fever, and the leukocyte count was moderately elevated.



Fig 21 Case 10 Local small intestinal ileus in a patient with pelvic inflammatory disease.

A survey film of the abdomen showed two sharply distended loops of small intestine, presumably ileum from their position and lack of distinctive markings, in the mid abdomen. The two loops together had a coffee-bean configuration. The markings between the loops appeared thickened, suggesting the presence of fluid.

The appearance of the loops was exactly the same in the film made in the erect position. They had not changed their configuration or position in any way. No fluid levels were present. Operation was advised, with the suspicion of local strangulation, even though the absence of fluid was against this possibility.

At operation, a bilateral salpingitis with a right ovarian abscess was revealed. Both tubes and the right ovary were removed. The distended loops of gut were not revealed through the incision, and because of the presence of pus, the surgeon elected not to explore the abdomen sufficiently to reveal them. The patient made an uneventful recovery, without any postoperative distention.

Fixation of loops of distended gut is usually interpreted as significant of strangulation or localized peritonitis, the latter being present in this case. The distention was certainly reflex in character, although the roentgen appearance—locally distended

loops without fluid—is seen in early mechanical obstructions as well.

2131 West Third St
Los Angeles 5 Calif

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DISCUSSION

Robert P Barden, M D (Philadelphia, Penna)

This is a difficult subject to present and I think Dr Osgood has done it in an extremely logical and well organized fashion I would like to discuss just two aspects very briefly

First of all, the most serious type of small bowel obstruction is apt to be the one with the fewest roentgen signs I am referring particularly to cases with strangulated loops of small bowel or mesenteric thrombosis, and I believe we should be aware of this pitfall and not assume that a case with minimal findings and an "acute abdomen" cannot be a case of serious intestinal obstruction

The second point I would like to emphasize is the danger inherent in the use of the Miller-Abbott tube Dr Osgood indicated that delay in decompression may be of more serious import to the patient's health than operation, even though the operation is performed when the patient is theoretically not in the best condition I am sure that I have seen patients who have died as a result of inadequate use of the Miller-Abbott tube who might conceivably have lived if the tube had not been used This is no criticism of the method, but it is a criticism of the way in which we as physicians may use it

In order to insure proper drainage and positioning of the tube, it is essential that a team, in hospital practice, of a physician and a nurse be assigned to all patients in whom the tube is passed Responsibility cannot be shifted from one service to another, and when the tube is in position, the maintenance of suction and proper use of both lumens in the tube are extremely important

It is a very common thing to have the tube passed adequately, have the patient returned to his room or the ward, and discover, the next morning, that the suction has been applied without opening the stopcock or to the wrong lumen of the tube There are so many factors in the mechanical use of the Miller-Abbott tube that require care that I cannot over-emphasize their importance

I do not believe that the Miller-Abbott tube should be used for decompression in patients in whom obstructions of the colon have been

diagnosed Very often back pressure in the colon will be sufficient to cause a perforation of the cecum before the tube reaches the lower ileum

I do not believe that the Miller-Abbott tube should be used in patients suspected of gangrenous small bowel obstruction, because these patients require immediate operation and any delay may be fatal

Ross Golden, M.D (New York City) I would like to comment on one point in Dr Osgood's paper, namely, the use of mercury in the balloon of the Miller-Abbott tube This was suggested by Dr F I Harris in an article published in 1944 (*A New Rapid Method of Intubation with the Miller-Abbott Tube*, J A M A 125 784-785, July 15, 1944) Before using it, I checked up with the Department of Pharmacology of the College of Physicians and Surgeons and with two or three of our internists about the possible dangers of absorption of metallic mercury They felt that no danger from this source existed We promptly adopted it at the Presbyterian Hospital in New York and since then have used it in at least 500 cases, if not more In the first case in which it was used, the mercury was injected by one of our younger surgeons who was particularly interested in the problem of ileus In so doing, he broke the balloon and the mercury was scattered through the small intestine No effect whatsoever could be observed Since then, in one or two other cases, a similar result has occurred I believe that we can dismiss the probability or practical possibility at least of deleterious effects from metallic mercury in the small intestine

We have found that the use of mercury assisted materially in getting the balloon through the pylorus It is not necessary to use as much as 8 c c, we have been entirely satisfied with 2 to 3 c.c. Furthermore, the weight of the mercury may be a handicap under certain circumstances One cubic centimeter of mercury weighs 13.55 gm and 2 c c weigh nearly an ounce As the tube is going through the stomach, the position of the patient must be such that the tip of the tube is pointing toward the pylorus and such that the mercury falls to the distal end of the balloon If the position of the patient is such that the mercury lies in the proximal end of the balloon, it may hold the tip back and may be a hindrance I can recommend the use of mercury as an aid in getting the tube through the pylorus

I agree with Dr Barden that it is well to have a nurse and somebody on either the Medical or Surgical Service particularly interested in this procedure At the Presbyterian Hospital we have a well trained nurse who inserts the tube and supervises the case as long as the tube is in the intestine In a recent publication I suggested that in many institutions it would not be practical to have such a nurse and that the best supervisor would be the radiologist because he would see most, if not all, of the cases This statement was mentioned in a review in the *Irish Journal of Medical Science* The reviewer (I suspect he was a surgeon) had the horrors at the idea that the Miller-Abbott procedure should be supervised by the radiologist However, I still believe the suggestion is good

SUMARIO

La Sonda de Abbott-Miller en la Obstrucción Intestinal

El empleo de la sonda de Abbott-Miller representa un importante adelanto en el diagnóstico y tratamiento de la obstrucción intestinal La descompresión del intestino distendido da lugar a un período más prolongado de preparación preoperatoria y puede transformar un caso de urgencia en un procedimiento electivo El alivio de la distensión simplifica la intervención y la presencia de la sonda, por impedir la distensión postoperatoria y resguardar y la línea de sutura, ayuda a obtener una convalecencia tranquila y merma la posibilidad de complicaciones En el vólvulo reflejo la sonda constituye un elemento terapéu-

tico en sí misma y ha logrado resultados brillantes En los procedimientos quirúrgicos que interesan el intestino grueso, el sondaje profiláctico ha resultado valioso, haciendo disminuir considerablemente la mortalidad operatoria El empleo de la sonda está contraindicado en la estrangulación y la gangrena intestinal, que exigen la intervención cruenta inmediata, así como en las hernias externas y las obstrucciones del intestino grueso

Expónese con minuciosidad la técnica de la introducción y manejo de la sonda a la vez que se describen los procedimientos de diagnóstico ejecutados con la introducción

de bario a través de la sonda, y que son principalmente útiles para determinar la presencia y grado de la obstrucción. No hay que atenerse a ellos como indicación o contraindicación de la operación, dado que algunas obstrucciones totales tal vez no exijan cirugía si, durante la descompresión, desaparecen los factores etiológicos, mientras que las obstrucciones parciales pueden persistir e imponer la intervención cruenta.

Cítanse estadísticas tomadas de la literatura que indican las ventajas del procedimiento y se analiza una serie de 53 casos de

obstrucción del intestino delgado, en 34 de los cuales se usó la sonda de Miller-Abbott. Agréganse las historias clínicas de 10 casos.

El radiólogo dotado de adecuada experiencia clínica puede cooperar con el médico que le envía el caso en la formulación de un diagnóstico temprano de obstrucción intestinal y cuando emplea la sonda puede hasta participar en el tratamiento, variando su misión de mera orientación roentgenoscópica a responsabilidad más o menos absoluta por la introducción y atención de la sonda.



Bagasse Disease of the Lungs¹

DAVID V LEMONE, M D, WENDELL G SCOTT, M D, SHERWOOD MOORE, M.D.,
and CAPT A. LINK KOVEN, U S P H S

BAGASSE is the name given to sugar cane after it has been crushed and the juice has been extracted. The term was originally used in Provence, France, to refer to the refuse from the olive-oil mills. Bagasse disease of the lungs, or bagassosis, is a pulmonary disorder brought about by the inhalation of dried bagasse dust. It is

bagasse are tough and possess insulating properties, which explains its use in the manufacture of acoustical and thermal insulating building boards and materials. More recently it has been used in the production of refractory brick.

Two factors are largely responsible for the lack of widespread information about

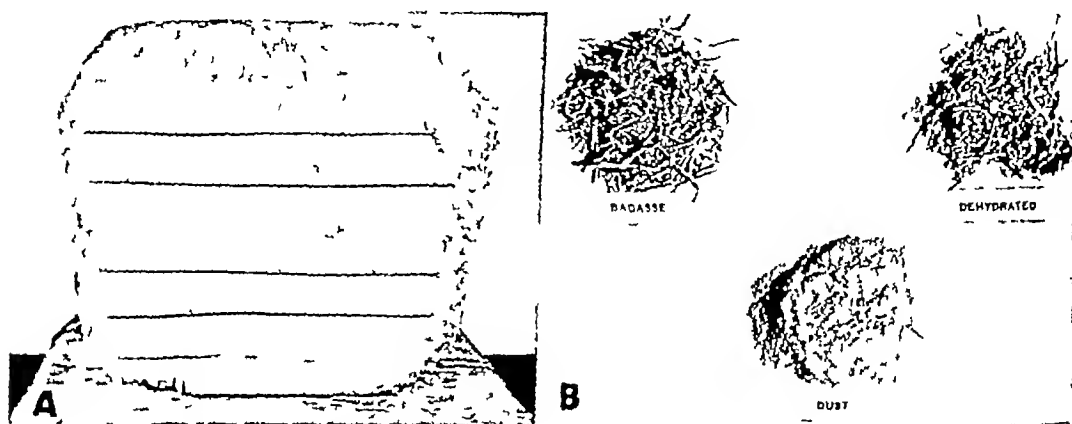


Fig 1 A The bagasse is shipped from Louisiana in tightly compressed bales. The first stage in processing it consists of breaking up the bales and grinding up the bagasse into small fibers or fine powder. This process is extremely dusty and is a serious industrial hazard unless special precautions against the dust are taken or the bales are broken up under water.

The photograph is of a bale of 'dehydrated' bagasse which is much less dusty and which is said to be less hazardous in handling.

B Three different forms of bagasse. 1 Bagasse as it appears when broken free from the bale. Notice that it is a mixture of large fibers and very fine dust particles. 2 A collection of bagasse dust which was removed from the rafters and beams in the grinding room. This dust is a very light fine brown powder. 3 Dehydrated bagasse has most of the fine particles of dust and dirt removed, leaving chiefly the larger fragments of cane.

a rare disease, with only some 30 to 40 cases reported in the medical literature, having been first described in 1941 by Jamison and Hopkins (8), of New Orleans.

So far as is known today, the disease occurs only in people who have been exposed to the inhalation of dried bagasse dust. Industrial engineers have been aware that exposure to the dust was an industrial hazard, but very few physicians are cognizant of this fact. The fibers of

bagassosis. In the first place, most of the reported cases occurred in men who handled bagasse derived from sugar cane grown in Louisiana, and the disease has been localized to certain communities. In the second place, men handling or cutting the finished products have not developed the disease because the heat and manufacturing processes destroy the fungi and bacteria as well as possible allergic protein, and the dust hazard in the modern fac-

¹ From the Mallinckrodt Institute of Radiology, Washington University School of Medicine, Saint Louis, Mo., and the Department of Radiology, Missouri University School of Medicine, Columbia, Mo. Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

TABLE I COMPOSITION OF TISSUES OF SUGAR CANE*

Constituent	Pith, %	Bundles, %	Rind %
Ash	1 08	3 58	1 64
Fat and wax	0 41	0 72	0 98
Protein	1 94	2 00	2 19
Pentosans	32 04	28 67	26 93
Celulose	49 00	50 00	51 09
Lignin	14 93	15 03	17 17

* From Browne, C A Chemical Composition of Bagasse Dust J Am Chem Soc 26 1221-1235 1904

tories has been largely eliminated. These conditions have restricted bagassosis to the communities which grow sugar cane and process it into sugar, such as Louisiana, or to the cities where the bagasse is manufactured into building board, as in England, or where it is used in making refractory brick, as in Missouri. Bagassosis also occurs in men employed in the Cuban sugar industry, where much dust is produced in handling sugar cane at the time it is cut. According to Manas (10) the Cuban disease is identical with that induced by the bagasse dust derived from Louisiana cane. In the Hawaiian Islands, bagasse is used for fuel, in a safe manner apparently, for we were unable to find reports of cases observed there.

Bagasse dust (Fig 1) consists for the most part of pith particles with some bundle and rind fibers. The chemical analysis of samples of bagasse varies slightly depending upon the virility and agronomic factors, such as the soil, fertilizer, etc. Hunter and Perry (6) state that bagasse yields from 3 to 4 per cent ash and that 50 per cent of the ash is amorphous silica. Also that microscopic and x-ray diffraction analysis of the ash yields 3 to 4 per cent silica. This is an insignificant amount, and even if the ash were 100 per cent silica, it would still be regarded as a nuisance dust. Hence, it is improbable that the minute quantity of silica is an etiologic factor in the development of bagassosis.

Table I gives the approximate chemical composition of the tissues of Louisiana purple cane on the basis of the percentage of dry matter, Table II gives the approxi-

mate chemical composition of bagasse obtained from Louisiana purple cane.

SYMPTOMS AND CLINICAL COURSE

The symptoms and clinical course of bagassosis are variable and depend largely on the length of exposure and the density of the inhaled bagasse dust. A bacterial and mycotic examination of bagasse is

TABLE II COMPOSITION OF CANE FIBER (BAGASSE)*

Cellulose	55%
Xylan	20%
Araban	4%
Lignin	15%
Acetic Acid	6%

* From Browne, C A Chemical Composition of Bagasse Dust J Am Chem Soc 26 1221-1235, 1904

difficult because it is a complex organic substance and has mixed with it dirt and fertilizer, is invaded by bacteria, and is subjected to fermentation processes while the sugar cane is lying in the open field. At present, Dr Morris Moore is undertaking these studies and has cultured several different kinds of fungi, as well as different bacteria, but his results are not yet available. To give a little idea of this problem, Hunter and Perry (6) estimated that 1 gm of the air-borne bagasse dust contained 240,000,000 fungal spores, and they isolated some twenty different species by culture methods.

A review of the various case reports brings out certain characteristic features. In general, about two months of exposure to the dust are required before symptoms appear, although the time has varied from three weeks to two years (14). The disease manifests itself as an acute febrile illness with extreme shortness of breath, a persistent cough with scanty mucoid sputum, and a profound weakness. The onset is insidious and gradual, for these patients usually do not realize that they are ill until they are seized by a sudden coughing spell and become so dyspneic as to force them to rest. The dyspnea is extreme. The patient described in Case I required oxygen for nearly two months. He was also cyanotic, but as a rule cyanosis appears in only the most severe cases. The usual ap-

pearance is that of a patient with a severe bronchiolitis and pneumonia

Patients with long exposures to heavy concentrations of the dust are critically ill. Among the 24 cases collected by Hunter and Perry (6) there were 2 deaths, a mortality rate of 8.3 per cent, which is sufficiently high to indicate that this is an industrial disease of a serious nature. On the other hand, most of the patients with only moderate or short exposure to the dust in light concentrations contract a less severe form of the disease, which usually clears up in two to six months.

PHYSICAL FINDINGS AND LABORATORY EXAMINATIONS

At the onset the fever may range from 37° to 39° or 40° C and persist for as long as two to three months before gradually subsiding. The pulse rate is correspondingly elevated. The respiratory rate is increased, ranging from 20 to 40. The supraclavicular and infraclavicular areas on the anterior chest wall may be retracted on inspiration. Percussion of the chest reveals a slight decrease in resonance. The breath sounds are not decreased, while the whispered voice may be increased, depending on whether or not areas of confluent consolidation have developed in the lungs. More important are the moist crepitant râles that are heard throughout both lungs. The cardiovascular system is unaffected. The mucosa of the nasopharynx is not injected. There is no enlargement of the lymph nodes, and the liver and spleen are within normal limits.

During the acute phase of the disease in severe cases, the white blood count may reach 16,000 to 20,000, in the moderately severe cases it may run around 10,000 to 12,000. As the pulmonary process clears, the number of white cells gradually declines and returns to normal. In the differential count there is a definite shift to the left, with the polymorphonuclear cells forming 70 to 90 per cent of the total. Of special note is the fact that an eosinophilia is usually present. The average eosinophil count in the 11 cases reported by Sodeman

and Pullen (14) was 3.5 per cent. In our Case I the eosinophils ranged from 4 to 8 per cent. The red blood cells and hemoglobin are not affected. The blood chemistry determinations are within normal limits. Agglutination tests for coccidioidomycosis, typhoid, etc., were all negative in our patients. Repeated attempts at culturing the sputum for fungi were also negative, as has been the experience of most other observers. Microscopic examination of the sputum did not reveal any abnormal cells or recognizable fungi or spores, but small highly refractile bodies were repeatedly seen in the sputum, and these may have been fragments of bagasse.

Examination of sputum concentrates has never revealed acid-fast bacilli. Injections of the sputum into guinea-pigs failed to produce evidence of tuberculosis. Urinalyses were always negative. The sedimentation rate was definitely elevated in Case II, a finding which has been reported by others.

RADIOGRAPHIC APPEARANCE

Radiographic findings in bagasse disease of the lungs are largely dependent on the duration of exposure to and the concentration of the bagasse dust. In patients who receive a prolonged exposure to heavy concentrations of the dust an extensive fine punctate infiltration develops throughout both lungs. In our series the most extensive pulmonary infiltration occurred in Case II. The punctate type of infiltration tends toward a nodular appearance as the disease begins to clear up. In the beginning, the infiltration is so dense that areas of consolidation develop, usually about the hilum and/or in the adjacent portions of the lungs. The infiltration pattern is not sufficiently characteristic to enable one to make a diagnosis of bagassosis by merely examining the film. In this disease one must follow the old dictum "There can be no radiographic diagnosis of bagasse disease of the lungs without a history of exposure to bagasse dust."

The one remarkable radiographic feature of this disease is that the process of pul-

monary infiltration, as observed on the roentgenogram, is a reversible one. This characteristic distinguishes bagassosis from the other pneumoconioses, in which a permanent fibrosis of the lung develops. Approximately two months are required from the time that the disease is at its height and exhibits the largest amount of infiltration in the lungs before appreciable resolution can be detected on the roentgenogram. By three months only minimal changes remain, and in five to six months the lung fields appear normal roentgenographically.

pathologic reports of the lung biopsies (Fig 2), which demonstrate cellular debris in the alveoli and in the bronchioles, and agrees to some extent with the clinical impression that these patients have an acute bronchiolitis and pneumonia. This patient (Case III) received an intermittent exposure to bagasse dust for over a year, but on removal from contact with the dust, his pulmonary symptoms disappeared and we presume that the findings in the roentgenogram did likewise, although a follow-up film was not made until a year

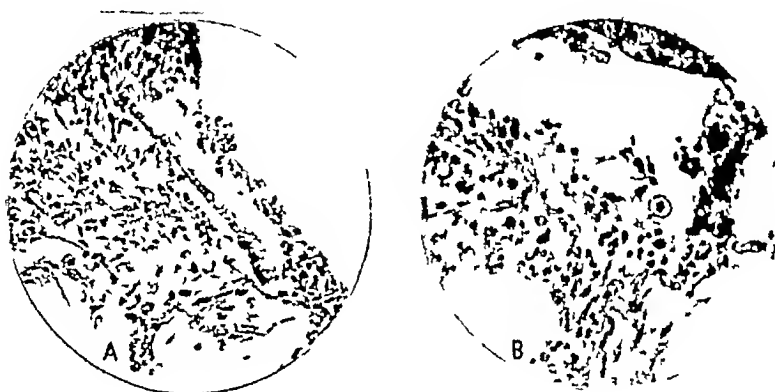


Fig 2 Photomicrographs of biopsy specimens of the lung obtained by aspiration through a large needle in the sixth and seventh week. These are the only pathological sections available for the study of the pulmonary changes in bagasse disease. They are reproduced from Sodeman and Pullen (14) who describe a fibroblastic reaction of the interstitial tissue with small needle like spicules of an irregular foreign material imbedded in the pulmonary tissues. The spicules are not numerous. Under the polarizing microscope these spicules rotated the plane of light and they appeared similar to particles of bagasse. These authors point out that the alveolar cells are numerous, very large, and possess a 'foamy' cytoplasm and in some areas fill the alveolar spaces.

This period of resolution can be well visualized by following the serial roentgenograms in Cases I and II, as reproduced in Figures 3 and 4, respectively.

Patients receiving short or intermittent exposure to bagasse dust in lighter concentrations may develop only a fine granular type of bronchial infiltration throughout both lungs, slightly heavier in the areas immediately about the hilum or, as in Case III (Fig 5), in the lower and medial portions of the left lung. On close examination, this type of infiltration bears a close resemblance to the fine lacy network that is sometimes formed by residual lipiodol in the alveoli. This is in conformity with the

later. At that time, the lung fields appeared to be within normal limits.

PATHOLOGY AND ETIOLOGIC FACTORS

Material for pathologic examination is limited, as only two deaths from bagassosis have been reported. Sodeman and Pullen (14) were fortunate enough to obtain sections from the lung of one patient at autopsy and from another by lung biopsy obtained with a 20-gauge needle. Photomicrographs of the biopsy specimens are shown in Figure 2. They are described by these authors as showing a fibroblastic reaction of the interstitial tissue with small needle-like spicules of an irregular foreign

material imbedded in the pulmonary tissue. The spicules were not numerous and averaged 2×8 microns. When examined under the polarizing microscope, they rotated the plane of the polarized light and, microscopically, appeared similar to particles of bagasse. The alveolar cells were more numerous, were very large, possessed a "foamy" cytoplasm, and in some areas filled the alveolar spaces. The authors summarized these observations by saying that the pulmonary changes appeared to represent an organic pneumoconiosis.

The exact etiology of bagasse disease is obscure, but one fact is certain, namely, that exposure to dried bagasse dust can initiate a pathologic process in the lungs. The mechanism by which these changes take place and the reaction induced by the bagasse remain unsolved. To date, the disease has not been reproduced in experimental animals. We have made several attempts to do this and are now constructing additional equipment with which we hope to be more successful.

In their study of this disease, Jamison and Hopkins (8) were able to grow a fungus from two sputum cultures on one patient, but they did not describe its type or characteristics. Castleden and Hamilton-Paterson (1), as well as Gillison and Taylor (4), failed to isolate a fungus from the sputum of their patients. Others and ourselves have cultured various fungi from the sputum but have considered them to be contaminants or not associated with the disease.

A pulmonary disease known as maple bark disease is caused by the inhalation of fungi which grow on dead maple trees that have been cut for over a year. The patients are dyspneic, lose weight, have a productive cough with varying amounts of sputum, and fever ranging to 103° F, with night sweats and substernal pain. The clinical picture and chest roentgenograms closely resemble those of bagassosis, but all efforts to identify a similar spore in bagasse dust have failed to date. In the opinion of Towey, Sweany *et al* (15) the reaction to the spores was due to a local toxic effect and

foreign body reaction combined with a delayed effect resembling protein sensitization in certain clinical and immunological aspects. Fawcitt (2) gives a long list of pulmonary mycotic infections that appear in agricultural workers, such as hay workers, grain workers, stablemen, cattle men, etc. Thus, the possibility that bagasse disease may be due to a fungus has some precedent in other diseases, but there is no clear evidence to support this idea at the present time.

Another possibility is that a bacterium in the bagasse dust may be the inciting factor, similar to that which appeared in the stained cotton of the 1940 crop that was used in the English upholstering and mattress plants where the workers were exposed to high dust concentrations from the cotton. Schnitzer *et al* (12) examined samples of the cotton and found a gram-negative bacterium which was the etiologic factor. This disease, however, required an exposure to the dust of only one to six hours and was characterized by a sudden onset with an acute phase lasting twenty-four hours, irritation of the nasopharynx, cough, chills and fever, with all the symptoms disappearing in a few days. In this way it is quite distinct from bagassosis, in which no specific bacterium has yet been isolated. It was further suggested that an endotoxic-like substance might be produced by the bacterium, and, that this, when inhaled, was the etiologic factor.

The first investigators to suspect an allergic reaction as the cause of bagassosis were Castleden and Hamilton-Paterson (1). They prepared four types of extracts from bagasse for intracutaneous injection. Three patients gave positive reactions, and a group of controls who did not have bagasse disease gave negative results with the saline extract. It was concluded that the acute phase of bagassosis is possibly an allergic response in the lungs to this antigen with, but more probably without, an infective element, also that the pathological process could be (a) a form of silicosis which supervenes upon the al-

lergic phase during or after the resolution of the latter, (b) a response on the part of the lung to the crystalline cellulose in the bagasse, (c) a chronic process of fibrotic nature occurring in tissues which have become edematous from their allergic response to the antigen

Sodeman and Pullen (13) repeated the tests conducted by Castleden and Hamilton-Paterson, using extracts made from bagasse according to their directions. Ingestion of these extracts produced similar reactions in all patients and controls, and the investigators concluded that the reactions were an irritative phenomenon due to the release of histamine and did not necessarily indicate a sensitization to bagasse

Allergic pulmonary disease is well known, such as the syndrome described by Löffler (9), the symptoms of which resemble those of bagassosis and include cough, fever, leukocytosis, eosinophilia, and an elevated sedimentation rate, while the chest radiographs reveal transient areas of consolidation that appear and disappear rapidly. Furthermore, these patients have attacks of asthma, only a few râles are present in the lungs, and the disease clears up in about a week.

From these studies, the possibility that bagasse disease may be an allergic pulmonary reaction *per se* or a contributing factor cannot be ruled out, but evidence in favor of this view is not very strong.

Tuberculosis does not need to be considered as an etiologic factor in the absence of tubercle bacilli and negative tuberculin tests.

In summarizing the etiologic factors of bagassosis, one must conclude that it is an acute bronchiolitis and pneumonia due to bagasse dust. Whether or not the pathologic reaction is due to fungi, bacteria, or a virus associated with the dust, or to an allergic response to the bagasse or its possible infectious agents or their products, or to some chemical or physical property of the dust, or any combination of the above, has not been determined and is still open for investigation.

TREATMENT

In view of the obscurity of the exact etiology of bagassosis, there is no specific treatment. Most of the patients have been treated symptomatically. There was no notable response among those in whom the "sulfa" drugs were tried or in the one case treated by penicillin. Oxygen has afforded some relief of the dyspnea in the more serious cases.

CASE REPORTS

CASE I (Fig. 3) R. R. H., a 27-year-old white, married, firebrick worker, was transferred to this hospital by ambulance on May 18, 1946. From 1942 until August 1945, the patient was in the Army. He had been overseas and had served in North Africa, Sicily, and Italy. He was returned to this country in 1945 and was discharged in August in good health.

In January of 1946 he started working for a firebrick company. His work consisted of breaking up bales of bagasse that had been shipped from Louisiana and shoveling it into a "shredder," a machine that breaks up the larger bundles of bagasse and grinds it into a fine powder. This operation was conducted in a room with one side open to the outside but it was extremely dusty even when the bagasse was dampened with water or mixed with wet sawdust. The patient usually wore a mask which covered his nose and mouth, but at times he removed the mask and received numerous exposures to the dust without any protection.

About the first of April, after three and a half months of exposure, a dry, hacking cough developed and by the middle of April the patient was dyspneic on even mild exertion. At that time he experienced two chills on successive nights, and on coughing he brought up small to moderate amounts of foul, black, watery sputum which, he said, contained black specks of bagasse. The sputum continued to be of this type for only a few days and then became mucopurulent, containing a few specks of blood, it amounted to approximately one-third of a cup per day. At the same time the patient became very weak and could hardly get out of bed. Fever began at the time of the chills and persisted throughout the course of the illness.

On April 19, the patient entered a local hospital and an x-ray examination was made of his chest, revealing an extensive bilateral infiltration of both lungs, which was described as a "snow storm." He remained in the hospital about one month, during which time he received penicillin and oxygen, but he continued to become weaker. The chills and fever persisted and he had profuse night sweats. His weight decreased from 160 to 130 pounds. On May 18, 1946 he was transferred to this hospital for

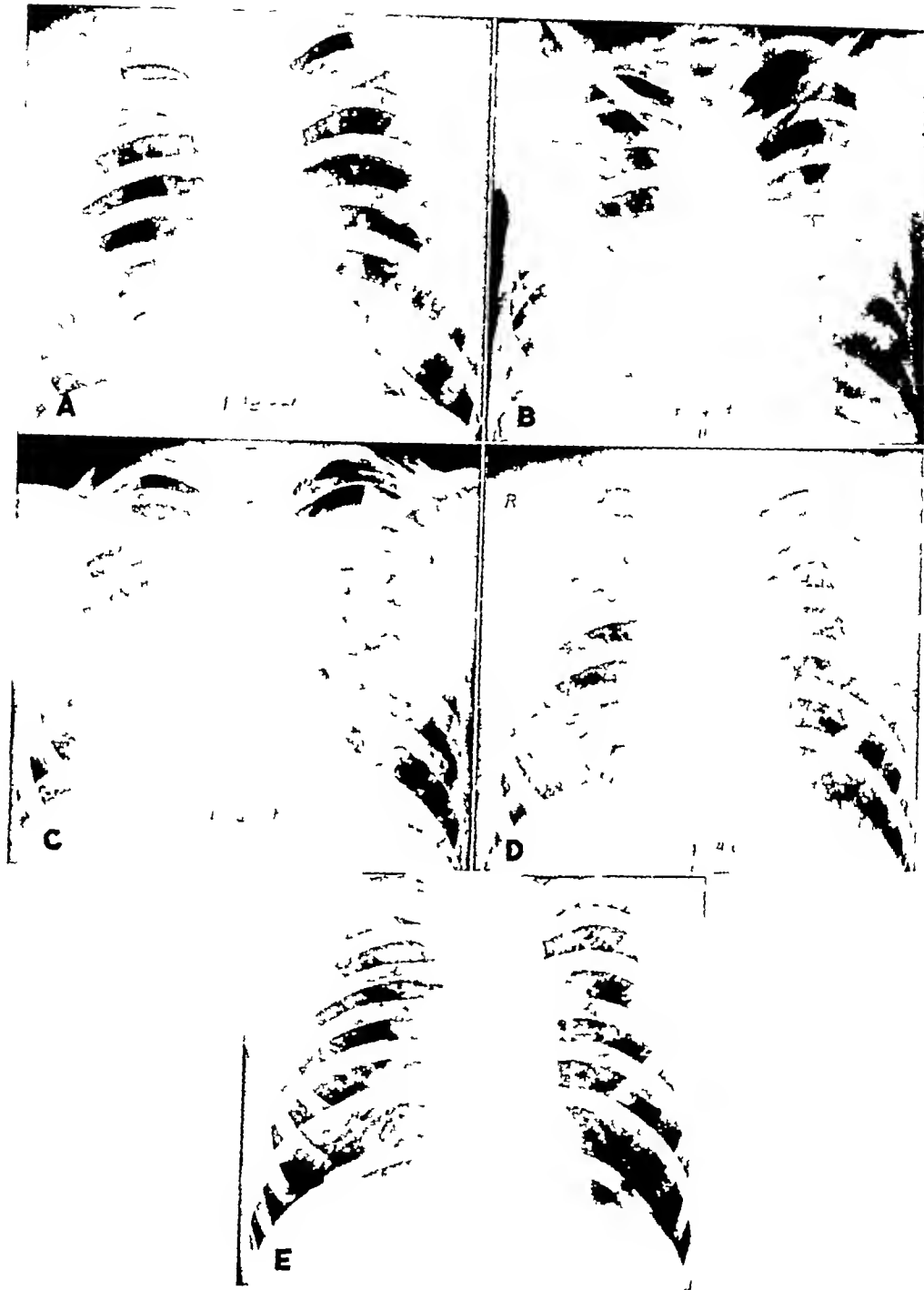


Fig 3 Case I Typical course of acute bagasse disease of the lungs showing the changes that take place in the lung over a period of approximately six months

A The pre-employment film which was considered to be normal

B Film made approximately one month after the patient became acutely ill following a period of three and a half months of exposure to bagasse dust. Note the symmetrical distribution of the small punctate areas of pulmonary consolidation and the peribronchial thickening in both lungs. The greatest change is about the hila and in the middle thirds of both lungs. The initial film made in April 1946, was not available for reproduction but appeared approximately the same. The patient was extremely ill and required continuous oxygen therapy.

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further study. On admission he had a temperature of 39.3°C , pulse 104, respirations 24, and blood pressure 110/78. He was dyspneic and orthopneic. He appeared acutely and chronically ill and was receiving continuous nasal oxygen. He did not complain of pain. He was not cyanotic.

Examination of the chest revealed marked retraction of the chest wall in the supraclavicular areas on inspiration. The percussion note was dull over the entire thorax. Tactile fremitus was unchanged. The breath sounds were loud, and many dry and coarse râles were heard in all areas. The whispered and spoken voice sounds were somewhat diminished. The heart was within normal limits. The rhythm was regular and the sounds were of good quality. The abdomen was slightly distended, the liver was slightly enlarged, the edge of the spleen could be felt. No other findings were obtained on physical examination.

The reports of the blood studies were as follows: red blood cells 5,000,000, white cells 18,150, hemoglobin 13.5 gm, differential count, basophils 0, eosinophils 8, juveniles 3, stabs 7, segmented polymorphonuclears 67, lymphocytes 11. The sputum was white, frothy, and mucoid. On microscopic examination it was reported that several refractile bodies were seen, but no one was able to identify them. Repeated examinations of concentrated sputum specimens were all negative for acid-fast bacilli. Repeated cultures of the sputum were negative for fungi and contained only those organisms that are usually present. Urinalyses were all within normal limits. The blood Kahn reaction was negative. A culture of the blood failed to grow any organisms. Blood chemistry analysis, including theicterus index, was within normal limits.

Skin tests were made with 1,000-unit extracts of several molds, including *aspergillus*, which gave immediate negative reactions. A skin test for coccidioidomycosis with 0.1 cc of 1:1000 dilution was negative at both twenty-four and forty-eight hours. The electrocardiogram was within normal limits.

By the first of June the patient began to feel better. His temperature dropped to normal. The respiratory rate decreased. A chest film made at this time revealed the same type of miliary infiltration throughout both lungs, but to a less extent than the original film made at the time of his admission to the first hospital in April. It was necessary to keep him supported with oxygen, as other-

wise he became very dyspneic and was troubled by a constant cough. His extreme weakness persisted. He was treated symptomatically, and penicillin was continued empirically through June 6, but it is doubtful if it was effective in the treatment. It was used because the patient was seriously ill and his clinical picture suggested a pneumonia or pulmonary infection. The white blood count had now dropped to about 13,000.

By July 5 the patient was able to get along without oxygen and to be up in a wheel chair. Only a few râles persisted throughout the lungs. He was coughing less and was gaining back his strength. The vital capacity was determined at this time and amounted to 1.8 liters, which was about 42 per cent of normal. This increased to 2.0 liters by July 11, at which time the patient was discharged. He returned to his home and continued to gain strength. The non-productive cough persisted, and on Oct 7, without any apparent reason, he coughed up about a cupful of bright red blood. He was sent back to the hospital on Oct 27 for a bronchoscopic examination. This was done by Dr A. C. Stutsman, who was unable to find any bleeding point or source of the hemorrhage. He mentioned that the bronchi appeared to be thickened and grayish in color, with slight injection of the mucosa. A small amount of seromucoid secretion was present in the main bronchi. The vital capacity was retested and had now increased to 3 liters. The venous pressure was 108 mm of saline. The circulation time (arm to tongue) was 15 seconds with decholin.

CASE II (Fig 4). E. L., a 42-year-old married colored laborer, had worked for the same brick company as the man reported in Case I. His family history and past history are irrelevant. From August 1943 to Feb 29, 1944, he worked in the dry press department where he was subjected to light exposure to silicate dust with very minimal free silica. He was discharged because of absenteeism. On April 4, 1944, he was rehired and worked in the insulation department, where he was exposed to ground dry bagasse dust until June 29, 1944, an exposure of eleven weeks. He had no previous history of any respiratory condition or pleurisy and had never been sick before this present illness.

In the middle of May 1944, this man experienced an acute coughing and choking spell in the company cafeteria. He also noticed that he was somewhat

C. The heavy areas of consolidation have undergone partial resolution. Note the fine granular shadows that correspond to consolidation in the air sacs of the lungs. The patient was now feeling better but it was necessary to keep him supported with oxygen.

D. This film was made two weeks after discharge from the hospital and shows practically complete resolution of the miliary consolidation in both lungs. The patient was now able to be up and about but was still weak and coughing.

E. On Oct 7 this patient coughed up a cupful of bright red blood. A bronchoscopic examination failed to reveal the bleeding point or source of the hemorrhage. The bronchial mucosa appeared to be normal and free of any excessive secretion. The vital capacity had increased to 3 liters. Venous pressure was 108 mm of saline and the circulation time was 15 seconds with decholin. The patient had gained weight and within a few months was doing light work.

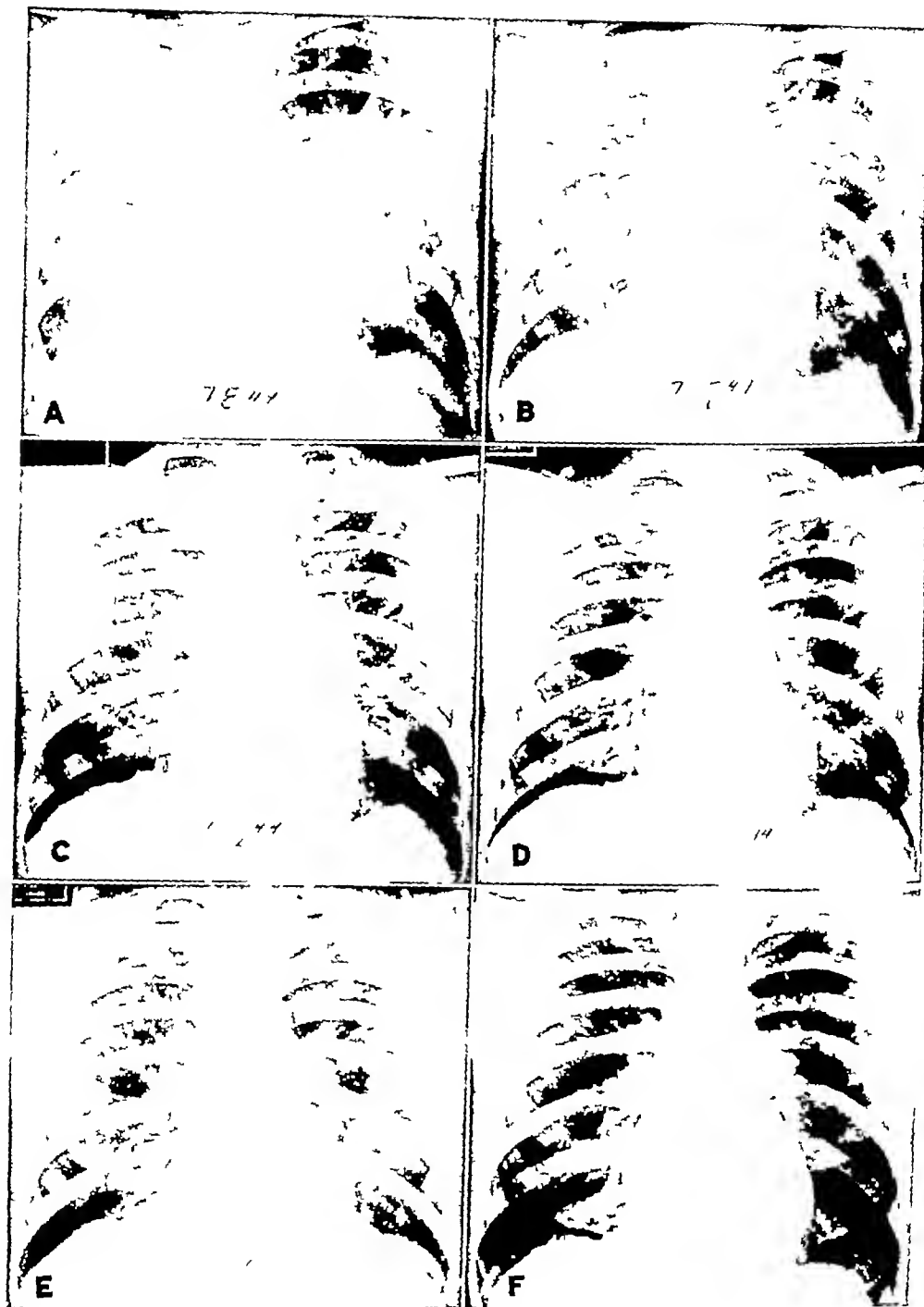


Fig 4 Case II Typical pulmonary changes in bagasse disease of the lungs with ultimate resolution
 A The patient had been ill for two months prior to taking of this film Note the bilateral involvement of the lungs greatest about the hila Areas of consolidation are present in the adjacent areas of the lungs The characteristic features are the small patchy areas of consolidation in the smaller divisions of the lobules
 B Definite resolution began to take place within the next two weeks although the patient only brought up small amounts of clear mucoid material He was now beginning to feel better but was still quite ill
 [Legend continued on opposite page]

short of breath on exertion and realized that it was more difficult for him to do the manual labor that was required in his job. Shortly thereafter, he consulted a private physician, who had x-ray films made of the chest. These revealed an extensive miliary type of infiltration throughout both lungs, with areas of conglomeration and consolidation immediately about the hila. Fever was noted at this time.

On July 24, 1944, the patient was admitted to a sanitarium. Upon admission it was reported that he was dyspneic, with a temperature of 99.2°F , pulse 116, and respirations 28. He had lost about 25 pounds in weight. It is interesting that he thought his illness had developed gradually over a period of several months. He had repeated night sweats. He described the onset as characterized by cough, pain in the chest, and the spitting up of some blood, accompanied by chills and fever, with shortness of breath and a gradually increasing weakness.

On physical examination the patient appeared to be in a fair state of nutrition. The heart was within normal limits, but the rhythm was irregular. Blood pressure was 120/94. Many fine crepitant râles were heard over both lungs. The breath sounds were increased, as was the whispered voice.

Repeated sputum examinations were negative for acid fast bacilli. The blood Kahn reaction was negative. Guinea-pigs were inoculated with the sputum on Aug. 10, 1944, and again on Oct. 21, 1944. Both animals were sacrificed, autopsied, and were negative for tuberculosis. The sputum was also cultured and was negative for fungi. On July 29, 1944, the vital capacity had fallen to 2.35 liters. The sedimentation rate was 22. Urinalysis was within normal limits.

From the time of his admission to the hospital until the middle of August, the patient had a fever ranging from 98° to 101°F . He was treated symptomatically and on about the same regime as patients with tuberculosis in the sanitarium. He gradually improved, the sputum became scant, and there was a gain in strength and weight. On Feb. 4, 1945, approximately seven months later, he was able to be discharged. The infiltration in the lungs, as demonstrated in the chest films, gradually cleared.

On May 25, 1945, the patient returned for a checkup. At that time he had no sputum, no cough, no chills, and no fever. He had nearly regained his strength. He had done no work since leaving the hospital and had been convalescing at home. Chest films at this time revealed only coarse markings, with little residue of the initial infection.

CASE III (Fig. 5) O. G., a 30-year-old white married laborer presents an interesting case, as he had only moderate pulmonary involvement as demonstrated roentgenographically. He gave a history of the usual childhood infections, as well as pneumonia. In 1941 he had a duodenal ulcer which continued to cause him trouble intermittently to the time of admission. During the x-ray examination of the gastro-intestinal tract the chest was observed fluoroscopically and was reported as negative. Early in 1944 he contracted undulant fever from which he recovered uneventfully.

Prior to his employment at the brick company, the patient worked for a year and a half in a coal mine. From 1939 to 1943 he was employed by a firebrick company in a position where he was exposed to moderate dust concentration of silicates. Late in 1943 he was transferred to another department, where he received intermittent exposure to a fairly heavy concentration of bagasse dust for about one year. At the end of that time, late 1944, he suffered from a cough which was non-productive, complained of slight substernal pain, was dyspneic on exertion, and felt weak. He continued to work, and his record shows that throughout his entire period of employment he never lost a day from sickness. He consulted a physician on Sept. 18, 1944, at which time a chest film was made. This physician reported exaggeration of the hilar markings, with a diffuse pulmonary fibrosis and a disseminated pulmonary infiltration throughout both lungs of an unusual type. The physician requested a more complete history with reference to dust and respiratory hazards. The patient was then transferred from the plant and given a position as a clerk, where he no longer was exposed to dust. His symptoms continued, and on Oct. 19, 1944, stereoscopic films were made of the chest and were interpreted as demonstrating a pneumoconiosis.

The symptoms gradually disappeared and the patient's strength increased. Another chest film was made on Sept. 22, 1945, when the radiologist reported that the punctate infiltration in the lung fields was much less evident and that the pulmonary infiltration was of a reversible type, and again requested that a detailed study be made of the dust exposure to which this man had been subjected.

The subsequent review of the dates of this patient's exposure to the silicate dust and later to bagasse dust, with the development of his pulmonary illness and the reversible changes in the lungs, as demonstrated on the roentgenograms, was the first suggestion that this was a case of bagasse disease of

C. Small areas of pulmonary infiltration and peribronchial thickening remain in both lungs despite marked improvement. Cough was now non-productive and there was no fever or any other symptom.

D. Approximately eight months after the development of the disease the lung markings are still coarse. The patient still complained of weakness and shortness of breath but was able to be up and around.

E and F. About one year after development of the disease the lungs have regained their normal appearance. The patient felt well and was able to go about his routine duties.

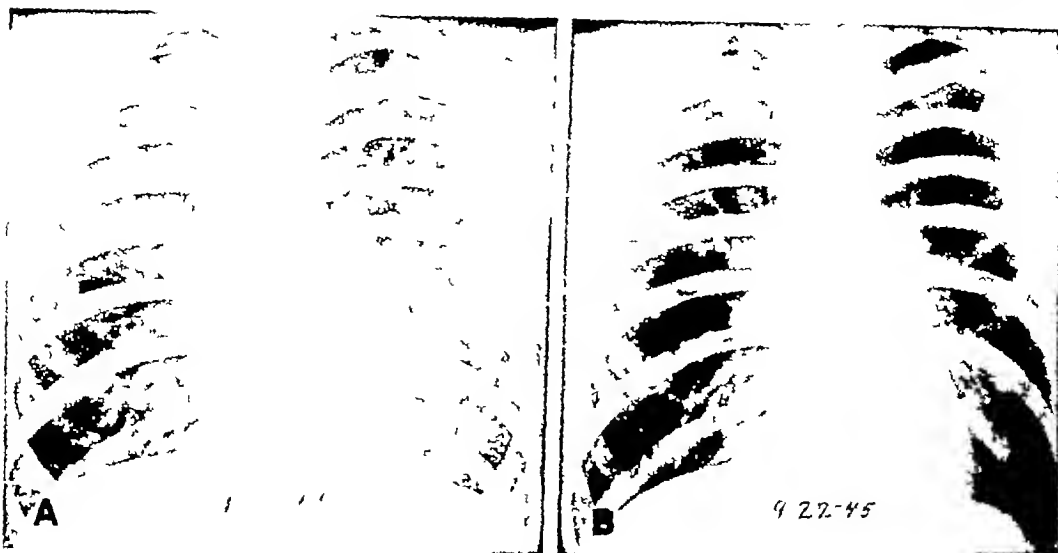


Fig 5 Case III Typical case of mild bagasse disease of the lung induced by intermittent exposure to a light concentration of bagasse dust over a period of one year

A After nearly a year of intermittent and light exposure to bagasse dust, this patient began to complain of a non productive cough, with weakness, slight substernal pain and shortness of breath on exertion. He continued to work and throughout his entire period of employment never lost a day from sickness. This film was originally reported as showing exaggeration of hilar markings, with a diffuse pulmonary fibrosis and a disseminated pulmonary infiltration of both lungs of an unusual type. The physician (D L) requested a full history with reference to dust exposure and respiratory hazards. The man was then transferred to a department free of bagasse dust.

B Approximately one year later, this man was re-examined because of the findings noted above. The radiologist now reported that the punctate infiltration in the lung fields was much less evident and that the pulmonary infiltration was of the reversible type and consequently was something unusual and not a typical pneumoconiosis. This observation was the stimulus for an intensive check-up on the patient's exposure to various dusts and led to the incrimination of bagasse dust.

the lungs. This was the first patient that had been recognized as having the disease in this community and focused our attention on this industrial hazard. Today this patient is well and symptom-free. His chest film is well within normal limits.

CONCLUSIONS

1 Inhalation of bagasse dust, derived from sugar cane after it has been crushed and the juice extracted, incites a pathologic process in the lungs which has been termed "bagasse disease of the lungs," or "bagassosis."

2 Information concerning bagassosis should be disseminated because bagasse is being used more extensively in the manufacture of thermal and noise-insulating building materials and in the manufacture of refractory brick. As such, it constitutes a serious industrial hazard unless properly handled.

3 Pulmonary changes incited by the inhalation of bagasse dust consist in a diffuse infiltration and consolidation, an acute

bronchiolitis or pneumoma, that is similar to that seen in pneumoconiosis but in one respect is greatly different. It is a reversible reaction, with the process undergoing resolution and the lung regaining its normal appearance on the roentgenogram.

4 The exact etiologic factors in bagasse disease of the lung are as yet unknown, and this problem is still open for investigation.

5 Three cases of bagassosis are reported, including a discussion of the symptoms, physical findings, laboratory reports, and clinical course.

Wendell G. Scott, M.D.
4952 Maryland Ave
St. Louis, Mo.

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DISCUSSION

Capt A Link Koven, U S P H S As pointed out, the exact etiology of bagasse disease remains obscure At least, we may conclude that bagasse may enter the alveoli and initiate a fibroblastic reaction and that by digestion and absorption, through the activity of cellular response, these changes are removed and a normal functioning lung (clear on x-ray examination) remains In view of the obscurity of the etiology of bagassosis and the lack of specific treatment, chief reliance at present is in the provision of a dust-free environment, introducing either proper exhaust ventilation and water spray or a change to a wet method of collecting and breaking the bales

Because of the industrial importance of the properties of bagasse, its use will extend to other purposes It can be anticipated that the incidence of bagasse disease of the lung will increase The U S Public Health Service is interested in promoting practices that will prevent this disease and also in determining its exact etiology

The small number of cases that have been recognized and described does not necessarily mean that the number of cases of this disease is limited On the contrary, the comparatively recent recognition of this entity and the lack of its differentiation from several other similar diseases have minimized its real incidence and significance It is of importance that the nature and diagnostic features of bagassosis be made widely known among industrial physicians and roentgenologists

SUMARIO

Bagazosis Pulmonar

La inhalación del polvo del bagazo que deja la caña de azucar después de triturada y privada de su jugo, evoca un proceso patológico en los pulmones, que ha recibido el nombre de bagazosis pulmonar o neumo-bagazosis

La patología pulmonar provocada por la inhalación del polvo del bagazo consiste en infiltración y hepatización difusas y bron-quiolitis o neumonía aguda, semejante a la observada en la neumoconiosis pero muy distinta en un sentido, pues se trata de una reacción reversible, en que el proceso ex-perimenta resolución y el pulmón recobra su aspecto normal en la radiografía

No se conocen todavía con exactitud los

factores etiológicos de la bagazosis pul-monar, y el problema está aun en vías de investigación

Preséntanse tres casos de bagazosis, con una reseña de la semiología, hallazgos ffsicos, informes de laboratorio y evolución clínica

Debe divulgarse la información dis-ponible acerca de la bagazosis, pues se va usando el bagazo cada vez más en la fabri-cación de materiales térmicos y anti-ruido para construcción, incluso ladrillos refrac-tarios al calor y al ruido, y en esa capacidad constituye un grave riesgo industrial a menos que se manipule debidamente

Symmetrical Calcification of the Cerebral Basal Ganglia

Its Roentgenologic Significance in the Diagnosis of Parathyroid Insufficiency¹

JOHN D. CAMP, M.D.

Section on Roentgenology, Mayo Clinic, Rochester, Minn.

IN 1939 EATON, Love and I (1) reported six cases in which symmetric calcification of the cerebral basal ganglia was observed roentgenographically. In two of these cases there was definite clinical evidence of spontaneous parathyroid insufficiency and tetany. In retrospect, our original case, which was reported (2) in 1938 would also seem to be an example of this condition, although the diagnosis was not established before death. The basic pathologic changes responsible for symmetric calcification of the cerebral basal ganglia have been noted by many writers since Bamberger's (3) and Virchow's (4) original observations in 1855. It was not until 1935, however, that the first report concerning the roentgenographic appearance *in vivo* was published. In that year Fritzsche (5) described the changes observed in roentgenograms of three siblings and Kasanin and Crank (6) presented the roentgenographic and postmortem findings in one case. None of these authors mentioned the presence of parathyroid insufficiency. The older literature contains reports of seven cases of parathyroid insufficiency (tetany) in which calcification of the basal ganglia was observed by pathologists (7-11). In most cases the process was marked and, if roentgenograms had been made, these would probably have presented the characteristics of symmetric cerebral calcification.

To date, at the Mayo Clinic, we have observed 12 cases of symmetric calcification of the cerebral basal ganglia in which there was definite clinical evidence of parathyroid insufficiency and tetany. In one, the calcification followed a thyroidectomy at the age of nineteen years, in the other 11, the disease was of the spontaneous type.

The pathologic basis for the roentgenologic changes is a colloid deposition in and around the finer cerebral blood vessels, with subsequent calcification of the deposits, which coalesce and form vascular sheaths and concretions (Fig 1). There is general agreement as to the involvement of the media and adventitia of the smaller arteries and the infrequency with which the veins are affected. When the process is extensive, the capillaries may be occluded but the lumens of the arteries are rarely narrowed (Fig 1 b). Ostertag (8) concluded that the deposited colloidal material occurs so frequently in the anterior half of the globus pallidus and in the dentate nucleus of the cerebellum that its presence to a slight degree, if not normal, is at least not unexpected. A marked increase in the degree and extent of the vascular process is likely to occur at any age, in either sex, and in response to many diseases, not all of which need produce neurologic symptoms. Calcium is always present microscopically to a considerable degree before it can be revealed by present roentgenologic methods. In 5 of the 12 cases presented herewith, deposits of calcium were observed roentgenographically in the deeper layers of the cerebral cortex as well as in the basal ganglia and cerebellum.

The pathologic changes have been most extensive and therefore are most likely to be detected roentgenologically in parathyroid insufficiency and other diseases characterized by mental deterioration with or without convulsive seizures or motor symptoms referable to the extrapyramidal system. Since adequate treatment of parathyroid insufficiency results in a marked improvement of the mental condition of the patient and stops the convulsions without

¹ Presented at the Thirty second Annual Meeting of the Radiological Society of North America, Chicago, Ill. Dec. 1-6, 1946.

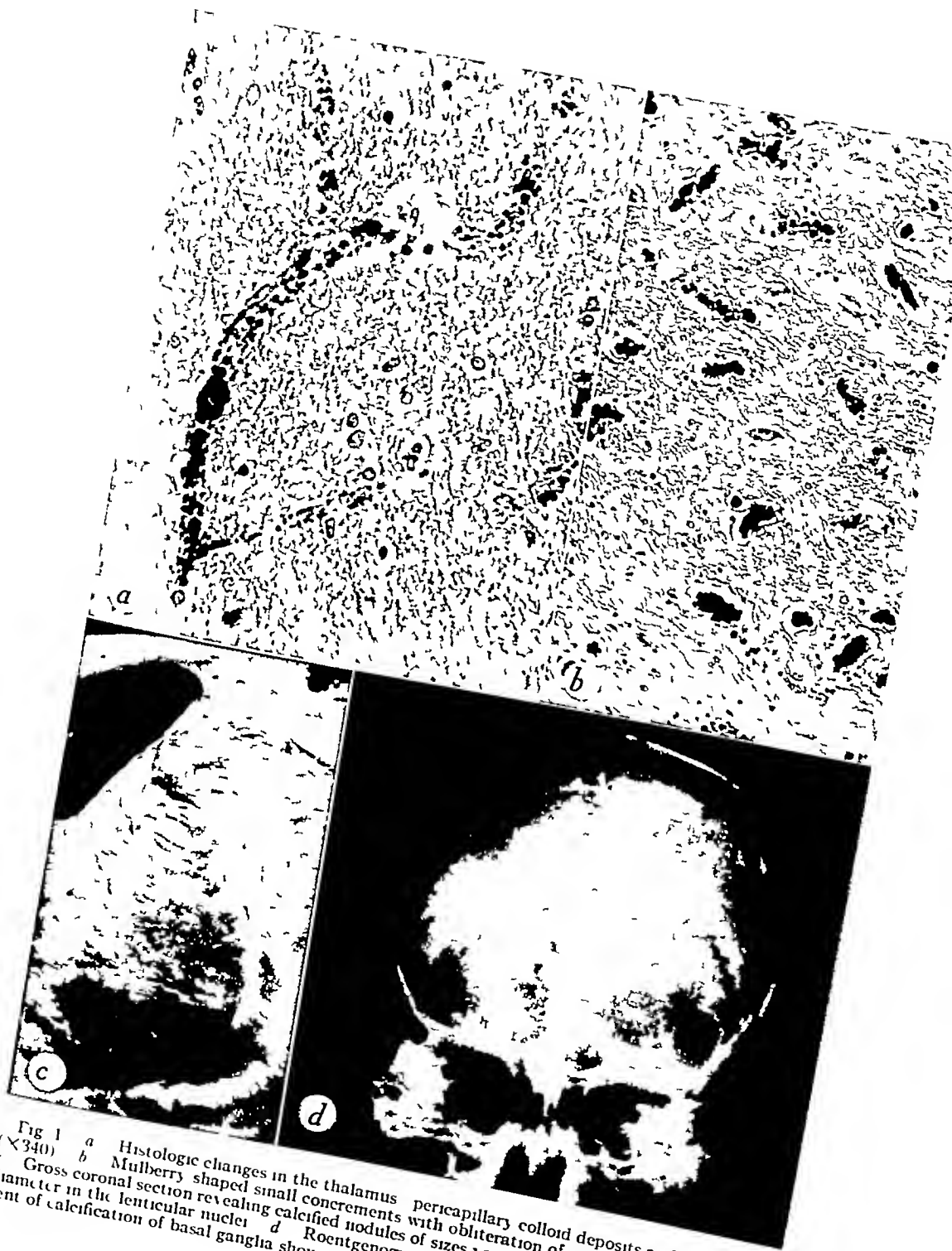


Fig 1 a Histologic changes in the thalamus pericapillary colloid deposits and calcification ($\times 340$) b Mulberry shaped small concretions with obliteration of capillary lumens ($\times 135$) c Gross coronal section revealing calcified nodules of sizes varying up to 3 mm in their greatest diameter in the lenticular nuclei d Roentgenogram revealing symmetrical distribution and extent of calcification of basal ganglia shown in a b and c

TABLE I CLINICAL AND ROENTGENOGRAPHIC DATA IN TWELVE CASES OF SYMMETRICAL CALCIFICATION OF THE BASAL GANGLIA

Case	Sex	Age years		Degree of Calcification as Determined Roentgenographically *		
		At Onset of Symptoms	When Observed at the Clinic	Basal Ganglia	Cerebrum	Cerebellum
1	F	6	27	+++	0	+
2	F	3	15	+++	0	0
3	M	19	42	+++	+	+
4	M	42 ¹ / ₂	44	++	+	++
5	F	6	32	+	0	+
6	M	7 ¹ / ₂	13	+++	+	0
7	F	39	42	++	+	++
8	F	7	19	+	0	0
9	M	11	19	++	0	0
10	F	2 ¹ / ₂	2 ¹ / ₂	0	0	0
			11	++	0	0
11	F	11 ¹ / ₂	28	+++	+++	+++
12	F	5	28	+++	0	++

* + = Minimal degree +++ = Maximal degree

producing roentgenographically detectable changes in the character of the cerebral or cerebellar calcification, it is apparent that the calcification itself is not responsible for the mental deterioration or convulsive phenomena (12)

SYMPTOMS

The symptoms in general include the various complications of chronic parathyroid insufficiency, namely, cataracts, convulsions, mental retardation, and trophic changes. In 3 cases tetany followed an attack of measles. Two of these patients were sisters, and the mother made the diagnosis of parathyroid insufficiency in the younger one because the symptoms were similar to those previously observed in the other. In one case (Case 10, Table I), in a girl two and a half years of age, the diagnosis of parathyroid tetany was made at the clinic in 1925. The values for the serum calcium as determined on two occasions at that time were 7.4 mg and 8.4 mg per 100 cc. Roentgenographic examination of the skull was reported as negative. The patient had no attacks for one month following treatment and at that time was taken home. Nothing further was heard of her until ten years later (1935), when she was brought back to the clinic because of her mental condition. Since the child did not like the medication, it had been discontinued soon after her return home in

1925. When seen ten years later, she was markedly retarded both mentally and physically, and convulsions were occurring frequently. The values for the serum calcium on two occasions were 6.4 mg and 6.0 mg per 100 cc. The value for serum phosphorus was 7.2 mg per 100 cc. Roentgenograms of the skull revealed symmetrical calcification of the cerebral basal ganglia. Because of her condition, the parents sent the child to a mental hospital for permanent care. It is interesting to speculate on how different the outcome might have been if the original prescribed medication had been continued. It is significant that in none of the 12 cases did a convulsion or "attack" occur after the institution of treatment for parathyroid insufficiency. Mental improvement was marked, and children previously retarded in school were able to keep up with their classmates and some have subsequently gone to college. These facts alone and the possibility of salvaging even a few of the mentally retarded and handicapped will justify the search for parathyroid insufficiency in the presence of roentgenographic evidence of symmetrical calcification of the cerebral basal ganglia.

ROENTGENOGRAPHIC FINDINGS

Symmetrical calcification of the cerebral basal ganglia produces a distinctly characteristic roentgen appearance (Fig 2)



Fig 2 Characteristic roentgenographic appearance of symmetrical calcification of the cerebral basal ganglia (spontaneous parathyroid insufficiency) *a* Bilateral symmetrical distribution of the shadows of calcification *b* Extent of shadows of calcification



Fig 3 Minimal calcification in the cerebral basal ganglia The symmetrical shadows of calcification shown in *a* might easily be mistaken for calcification in the choroid plexus The shadows of calcification are partially obscured by the density of the overlying shadow of the bone in *b*

Considerable variation in the degree and extent of this form of calcification may occur, corresponding to the stage of the disease at the time the roentgen examination is made. The first roentgen evidence of calcification consists in small, irregular, discrete, symmetrically distributed shadows of increased density in the region of the various basal ganglia, especially the putamen and caudate nucleus (Fig 3). When

the calcification is more marked, the irregular shadows take on a wavy linear appearance. This is especially obvious in the dentate nucleus of the cerebellum and in the folds of the cerebellar hemispheres (Fig 4). As the masses of calcium coalesce, the roentgen shadows become larger, denser, and more obvious (Fig 5). Coincident cerebellar calcification may be observed at any stage of the disease, as well as evidence

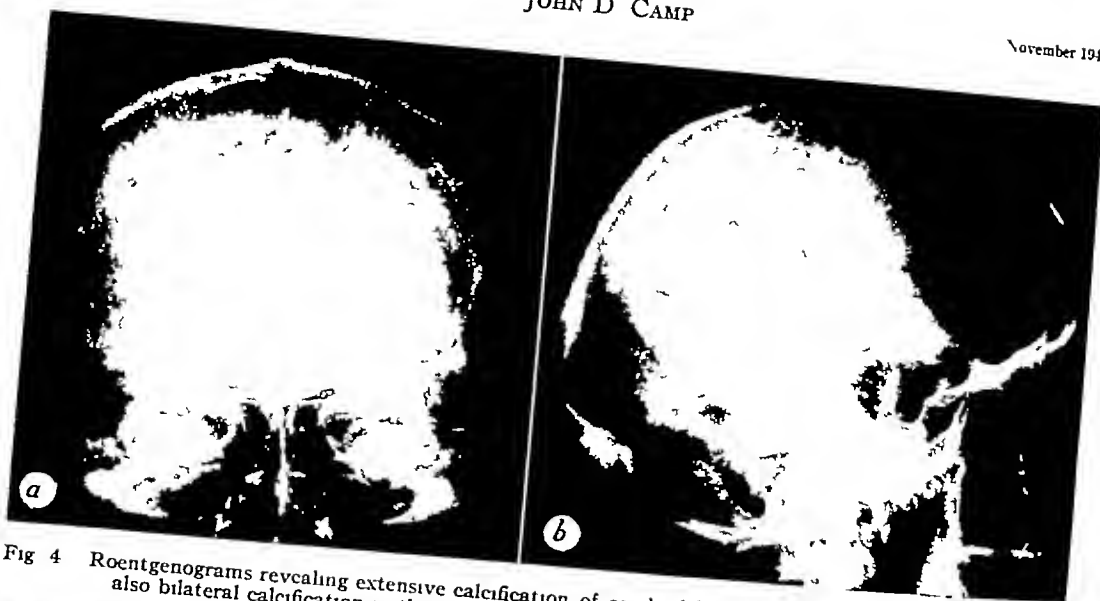


Fig 4 Roentgenograms revealing extensive calcification of cerebral basal ganglia and cerebellum. There is also bilateral calcification in the cerebral cortex. Spontaneous parathyroid insufficiency.

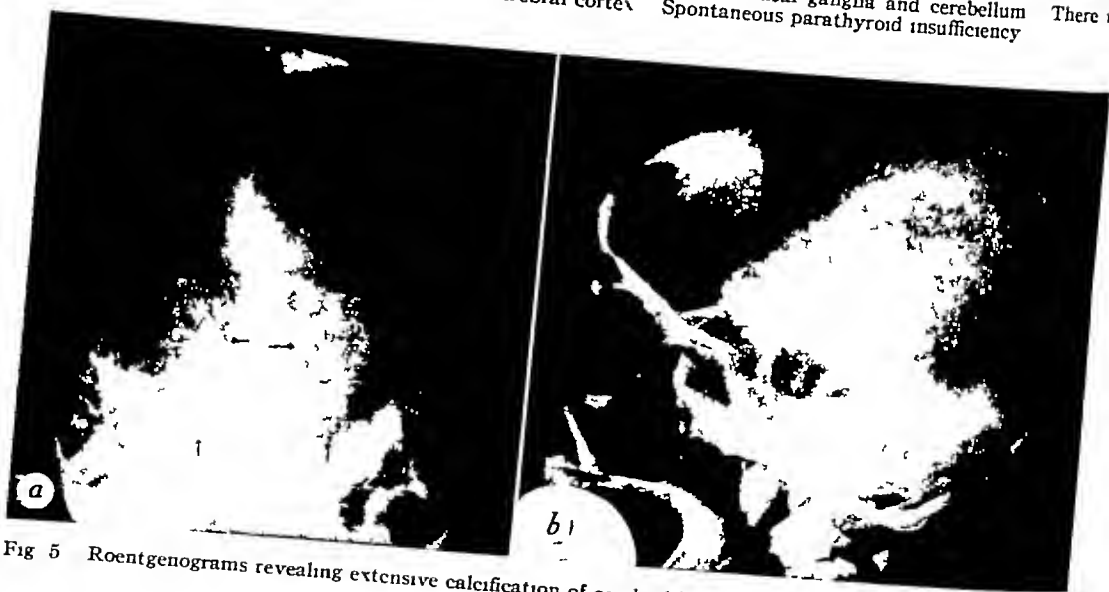


Fig 5 Roentgenograms revealing extensive calcification of cerebral basal ganglia. Postoperative parathyroid insufficiency.

of calcification in the deeper layers of the cerebral cortex. The latter may be so marked as to simulate a vascular lesion or calcified glioma.

Roentgenographically, it is important not to mistake the shadows of calcification in the ganglia for evidence of a neoplasm. The fact that the shadows are bilateral and symmetric is usually sufficient to exclude the possibility of tumor of the brain. If there is any doubt, pneumographic studies

may be carried out. With air in the ventricular system, the extraventricular position of the calcium shadows and their relation to the site of the basal ganglia will be well shown (Fig 6). In spite of the mental symptoms, there was no roentgenographic evidence of other cerebral abnormality in the 4 cases of our series in which pneumographic studies were carried out.

Calcium deposits within the choroid plexus of the lateral ventricles are com-



Fig 6 Pneumo-encephalograms revealing relation of lateral ventricles to shadows of symmetrical calcification in the cerebral basal ganglia Spontaneous parathyroid insufficiency Same case as Figure 2 *a* and *b*



Fig 7 Roentgenograms revealing extensive bilateral calcification of the choroid plexus This may be mistaken for calcification in the lenticular nucleus Roentgenograms also reveal a plaque of calcification in the falx cerebri

monly observed in roentgenograms of normal persons In certain anteroposterior roentgenograms, the bilateral shadows of calcification of the choroid plexus may simulate calcification of the basal ganglia However, when roentgenograms made in the lateral position are examined, the distinction between the two conditions should be obvious, since calcification of the choroid plexus is usually limited to the region of the genu of the lateral ventricle, whereas calci-

fication of the larger basal ganglia will be well anterior to this When calcification of the choroid plexus extends into the temporal horn on each side, it may be difficult to distinguish from calcification in the lentiform nucleus, although this seldom occurs without obvious calcification in the putamen and caudate nucleus as well (Fig 7)

As mentioned previously, calcification of the cerebral basal ganglia is not limited to



Fig 8 Roentgenograms revealing symmetrical calcification of cerebral basal ganglia and extensive calcification in cerebrum Encephalitis in infancy



Fig 9 Roentgenograms revealing symmetrical calcification of cerebral basal ganglia There are also nodules of calcification elsewhere in the cerebrum and massive calcification in the right lobe of the cerebellum Tuberous sclerosis

patients with parathyroid insufficiency In the course of this study, examples were observed in patients with a previous history of encephalitis, tuberous sclerosis, toxoplasmosis, and mental deficiency since

birth In one case in which the patient complained only of blepharospasm, there was no obvious cause for the presence of the calcification In another case, in which the calcification was of minimal de-



Fig 10 Roentgenograms revealing irregular nodular masses of calcium more or less symmetrically distributed in cerebrum, basal ganglia, and dentate nuclei of cerebellum. Toxoplasmosis in infancy. Identical twin brother had same condition.

gree, a mild hyperthyroidism and a positive Kahn test were the only positive clinical findings.

Patients with a previous history of encephalitis and evidence of calcification of the basal ganglia in almost all instances had evidence of other discrete areas of calcification throughout the cerebrum (Fig 8). This was most obvious in infants, in whom the age, abnormalities of the calvarium, and wide distribution of the shadows of calcification at once suggested a diagnosis other than parathyroid insufficiency.

In tuberous sclerosis, calcification of the basal ganglia when present was always accompanied by nodules of calcification elsewhere in the brain. The latter predominated (Fig 9).

In the presence of toxoplasmosis, the calcification in the basal ganglia appears to be very extensive, the calcium occurring in large, dense, irregular masses surpassing any changes observed in parathyroid insufficiency. Calcification of the dentate nucleus is usually very marked and, in addition, multiple discrete irregular nodules of calcification are distributed throughout the cerebrum (Fig 10). The age of the patient and the evidence of disease at or soon

after birth should assist in the proper diagnosis.

Two patients with mental deficiency dating from birth exhibited symmetric calcification of the basal ganglia that could not be distinguished from that observed in parathyroid insufficiency (Fig 11). There was no clinical evidence of parathyroid dysfunction in either case, and the values for the serum calcium and serum phosphorus were normal.

In the course of this study two patients with unilateral calcification of the basal ganglia of minimal degree were observed. In both cases the calcification was disclosed by roentgenograms made routinely for trivial and unrelated symptoms. There was no evidence whatever of neurologic or parathyroid disease in either instance.

COMMENT

It is evident from this study that parathyroid insufficiency is only one of several diseases producing a disturbance of cerebral metabolism which results in the deposition of colloid material in and about the finer cerebral vessels with subsequent calcification. The basal ganglia and dentate

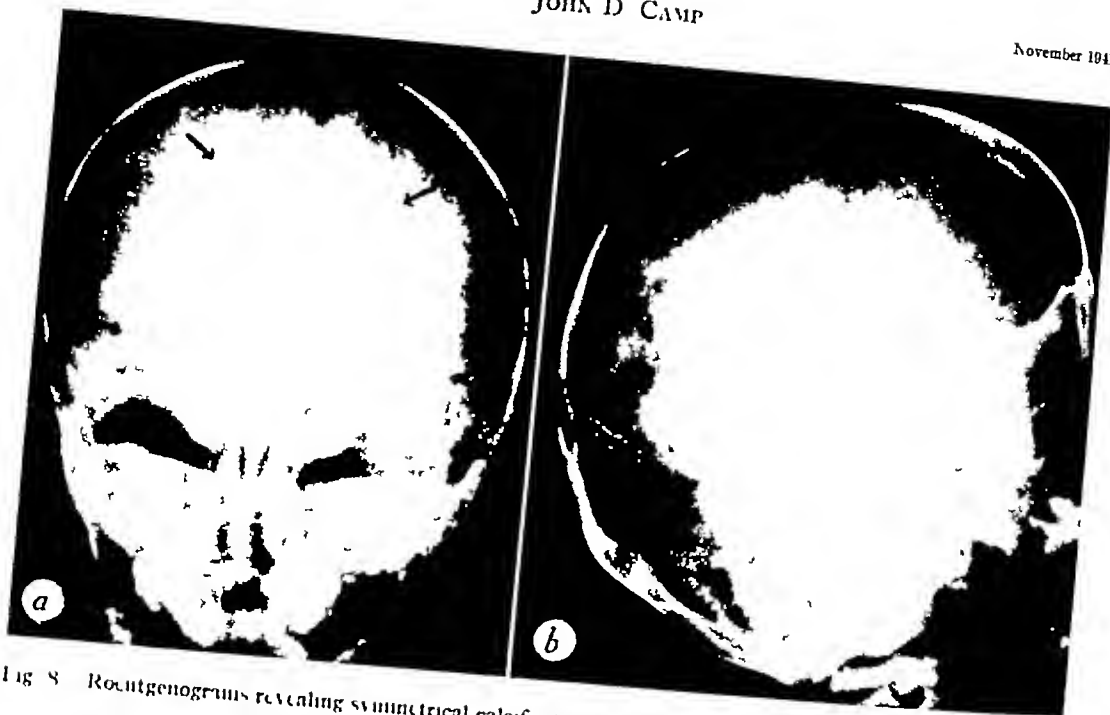


Fig 8 Roentgenograms revealing symmetrical calcification of cerebral basal ganglia and extensive calcification in cerebrum. Encephalitis in infancy

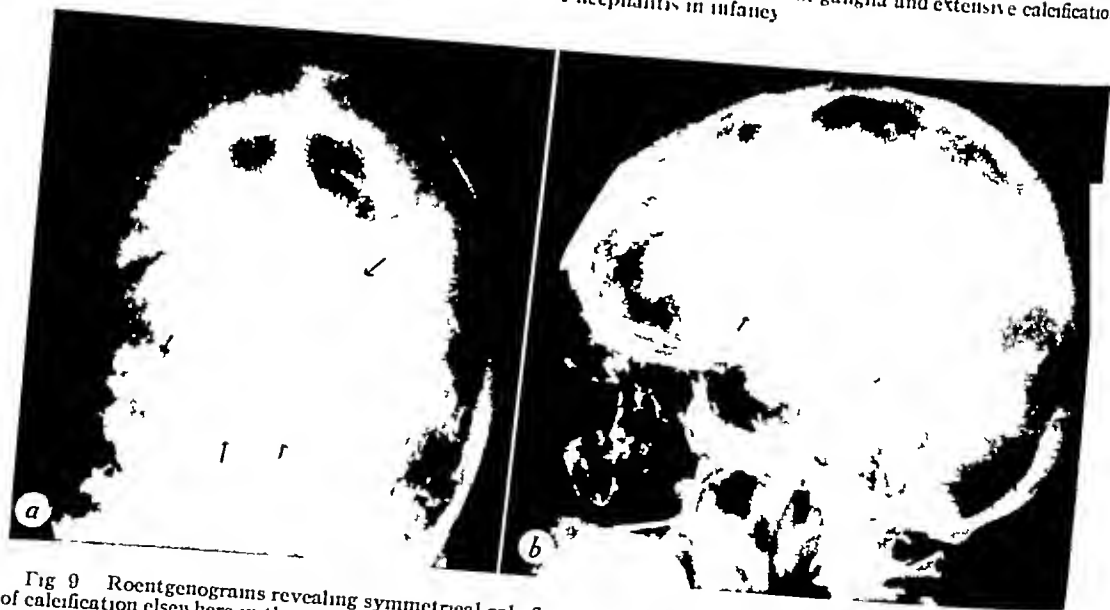


Fig 9 Roentgenograms revealing symmetrical calcification of cerebral basal ganglia. There are also nodules of calcification elsewhere in the cerebrum and massive calcification in the right lobe of the cerebellum. Tuberous sclerosis

patients with parathyroid insufficiency. In the course of this study, examples were observed in patients with a previous history of encephalitis, tuberous sclerosis, toxoplasmosis, and mental deficiency since

birth. In one case in which the patient complained only of blepharospasm, there was no obvious cause for the presence of the calcification. In another case, in which the calcification was of minimal de-

12 EATON, L M , AND HAINES, S F Parathyroid Insufficiency with Symmetrical Cerebral Calcification, Report of Three Cases, in One of Which the Patient was Treated with Dihydrotachysterol J A M A 113 749-752 Aug 26, 1939

DISCUSSION

Joseph C Bell, M D (Louisville, Ky) I am certain that we all recognize the very real contribution that Dr Camp has made this afternoon in the study of some diseases with cerebral manifestations Many are familiar with the work reported in the literature showing a high incidence of degenerative changes in the basal nuclei in individuals who have died from various causes We also know that in most of these there was no reason to suppose that there was any correlation between the symptoms presented prior to death and the calcification in the basal nuclei

My interest in symmetrical cerebral calcification dates from 1928, when I saw the films of a

patient with this very characteristic type of cerebral calcification I was not familiar with the cause or significance of the calcification but was quite certain that it was not in the choroid plexus nor in any type of cerebral tumor I recognized its real nature and significance only after the work of Dr Camp and his associates was published Any one familiar with the characteristics of this particular type of calcification would not mistake it for calcification in a cerebral tumor

Dr Camp now makes a contribution of even greater significance He brings us knowledge of a group, small though it may be, in which there was no hope for recovery in the past but in which recovery, with the chance of leading a useful and more or less normal life, is now not only a possibility but a probability It would seem to me that this group is larger than appears at present, and I believe that, if our method of examination is that outlined by Dr Camp, many more than 12 cases will be reported in the next decade

SUMARIO

La Calcificación Simétrica de los Ganglios Basales del Cerebro en la Insuficiencia Paratiroidea

La insuficiencia paratiroidea es una de varias dolencias que, trastornando el metabolismo cerebral, da por resultado el depósito de sustancias coloides en los vasos cerebrales más delicados y en la vecindad de los mismos, con calcificación subsiguiente Los patólogos han reconocido desde hace tiempo que los ganglios basales y el núcleo dentado son asientos predilectos de dicho proceso En la Clínica Mayo han observado 11 casos de calcificación simétrica de los ganglios de la base del cerebro, asociada a signos clínicos bien definidos de insuficiencia y tetania paratiroideas espontáneas Dada la rareza de la insuficiencia paratiroidea espontánea y la observación de

estos 11 casos de calcificación simétrica de los ganglios basales, debe recalcar la asociación de los dos estados y en todo individuo con insuficiencia paratiroidea crónica debe hacerse un examen roentgenológico del cráneo Además, hay que determinar la concentración del calcio sérico para establecer o excluir la insuficiencia paratiroidea en todo caso en que las radiografías muestren calcificación simétrica de los ganglios de la base del cerebro La rápida respuesta a una terapéutica adecuada en esos casos y la posibilidad de rescatar así a algún enfermo mentalmente retardado o incapacitado justifican plenamente estos esfuerzos





Fig 11 Roentgenograms revealing symmetrical calcification of the cerebral basal ganglia Mental deficiency since birth no clinical evidence of parathyroid insufficiency

nucleus have long been recognized by pathologists as common sites of predilection for the process. Because of the rarity of spontaneous parathyroid insufficiency and the observance of 11 such cases in which symmetrical calcification of the cerebral basal ganglia was observed, I believe the association of the two conditions should be emphasized. It is possible that some cases of marked cerebral calcification associated with mental deterioration and convulsive seizures reported in the literature may have included a parathyroid insufficiency which was not detected. For this reason, all patients with chronic parathyroid insufficiency should have a roentgen examination of the skull. In addition, a determination of the concentration of serum calcium should be made to establish or exclude parathyroid insufficiency in all cases in which roentgenograms show symmetrical calcification of the cerebral basal ganglia. The prompt response to adequate treatment in such cases and the possibility thereby of salvaging an occasional mentally retarded or handicapped person or child should fully justify our endeavors.

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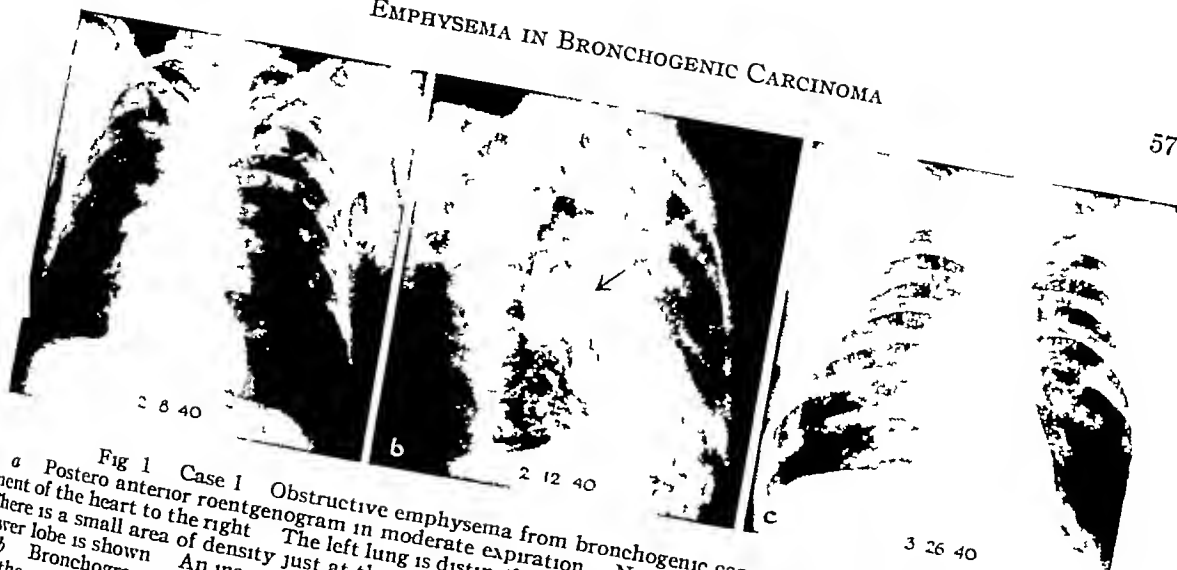


Fig 1 Case 1 Obstructive emphysema from bronchogenic carcinoma, left lower lobe
 a Postero anterior roentgenogram in moderate expiration Note elevation of right diaphragm and displacement of the heart to the right The left lung is distinctly more radiable than the right especially in the lower area There is a small area of density just at the apex of the heart Fairly typical obstructive emphysema of the left lower lobe is shown
 b Bronchogram An inspiratory film at this time appeared normal Note the ragged irregular, partially obstructing lesion in the left main bronchus just distal to the carina (arrow)
 c Postero anterior roentgenogram in inspiration, seven weeks later Characteristic emphysema in the left lower area is well shown indicating an inspiratory as well as expiratory emphysema at this time

findings are exactly similar to those seen with foreign bodies during the stage of obstructive emphysema. In this situation the diaphragm on the normal side ascends during expiration while on the abnormal side it remains in its inspiratory position. The mediastinum is displaced toward the normal side during expiration as well. The third stage described by Westermarck is that of complete stenosis. At this time the tumor has grown sufficiently, or accumulated sufficient debris or inflammatory products, to occlude the bronchus completely and thus produce the more commonly described atelectasis. The transition from obstructive emphysema to obstructive atelectasis can be observed if cases are followed for a period of time, as indicated in some of the cases reported below.

It should be noted that there occurs a stage in which there is inspiratory as well as expiratory emphysema. Westermarck (8) has recently described this stage and, therefore, now refers to four stages of bronchostenosis. Nevertheless, the observation of emphysema is best made during the phase of expiration, because the increased density of the normal lung which occurs during expiration makes the difference in radiability between the two lungs

more striking. Such an observation may be made during fluoroscopy, or on roentgenograms if films are made both in the inspiratory and expiratory phases.

It seems possible that the failure to observe this finding more often is the result of the custom of making routine x-ray examination of the chest by means of a single film or stereoscopic films exposed at the end of a deep inspiration. Routine fluoroscopy in all phases of respiration is seldom practiced. As will be seen from the case reports in this paper, it is often exceedingly difficult to detect the minor changes which are apparent during inspiration. Films made during expiration would be of the greatest value but are seldom made unless specifically indicated.

CASE 1 A man, aged 58, was admitted to the University Hospital, Feb 5, 1940. His health had been good until four weeks previously. At that time he began to cough and raised some blood-tinged sputum as much as 3 ounces being raised daily. There was also some hoarseness during the first week of his illness. He gave a history of periodic elevated temperature ranging from 101 to 103° F. There was no pain, and only moderate dyspnea but there had been a weight loss of 20 pounds. Physical examination showed evidences of weight loss. Percussion of the chest showed hyperresonance on the left but with complete absence of breath sounds—the typical signs of trapped air. A few

Emphysema An Early Roentgen

Sign of Bronchogenic Carcinoma¹

LEO G. RIGLER, M.D., and GJERT M. KELBY, M.D.

Minneapolis, Minn.

THE INCREASING incidence of carcinoma of the lung represents one of the urgent problems facing the medical profession. Whether this increase is real or relative, it is certainly true that the number of cases encountered seems to be greater each year. Surgical procedures have been developed to such a degree that the mortality has been reduced to as low as 5 per cent in one series (3), and five-year survivals after pneumonectomy are now in no sense rare. The importance of early diagnosis of bronchogenic carcinoma, therefore, is self-evident. For purposes of detection of the disease, to give the evidence which will lead to further investigation so that a definitive diagnosis may be made, x-ray examination is, without doubt, the only widely applicable method.

The possibilities and limitations of the roentgen examination in the diagnosis of carcinoma of the bronchus are well known and will not be considered here. We propose rather to describe an early roentgen sign which has been insufficiently stressed, namely, obstructive emphysema.

Although Nils Westermarck (6, 7) in 1938 first directed attention to the emphysema caused by the bronchostenosis accompanying bronchial tumors, it is notable and rather remarkable that there are so few references to such cases in the American literature.

Morlock (4) reported a case of carcinoma of the left main bronchus in which there was obstructive emphysema of the entire left lung. X-ray examination showed an enlarged left hilum shadow. Bronchoscopic examination revealed a new growth at the junction of the left upper and left main bronchi.

Cohen (1) reports a case in which atelectasis and obstructive emphysema caused by the same malignant neoplasm were co-existent in the same lung. The tumor was located in the main bronchus so that the orifices of the upper and middle bronchi were completely obstructed, while only a check-valve type of obstruction was produced in the lower bronchus.

Vinson (5) states that emphysema beyond the point of obstruction is rarely present in carcinoma of the bronchus. He does, however, report the case of a twenty-nine-year-old man with carcinoma of the bronchus associated with emphysema.

Westermarck (6) divided the effects of bronchostenosis into three separate stages similar to those described by Jackson (2) for foreign bodies. In the first stage there is diminution of aeration as a result of a minimal stenosis. Some impediment to the ingress and egress of air occurs and it is possible that there may be some decreased radiability of the affected lung. Cases in this stage are difficult to detect on x-ray examination and are rarely encountered.

The second stage occurs when the stenosis becomes of higher grade so that a check-valve action takes place. With the diminution of the bronchial lumen occurring during expiration, there is presented a much greater difficulty for the egress of air than for its ingress during inspiration. As a result, a type of relative emphysema affecting the abnormal lung occurs. The lungs may appear almost equal in aeration or in radiability in roentgenograms made during inspiration. In expiration, however, the abnormal lung retains its air while the normal one is deflated, causing a striking difference in their appearance. The

¹ From the Department of Radiology and Physical Therapy, University of Minnesota. Read by title at the Thirty first Annual Meeting of the Radiological Society of North America, Chicago, Ill., Nov. 9-10, 1945. Received for publication in June 1947.

the left upper lobe is clearly apparent. At the same time there is seen a moderate enlargement of the left hilum. Observation of these two findings at that time might have lead to a suspicion of the correct diagnosis and further investigation would have been carried on five months earlier than actually was the case.

The transition, in the left upper lobe, from emphysema to atelectasis is well

on Jan 8, 1945, with somewhat the same complaints, an x-ray examination of the chest was made (Fig 3, a) and interpreted as negative. Shortly after this an episode of fever occurred, and a diagnosis of left lower lobe pneumonia was made on the basis of physical findings and symptoms. The patient responded to chemotherapy and apparently recovered to some degree. On Feb 12 he experienced another episode of fever, pain in the left chest, cough, and weakness. At that time he was hospitalized elsewhere and a second film of the chest was made. This showed a mass in the left hilum, atelectasis of

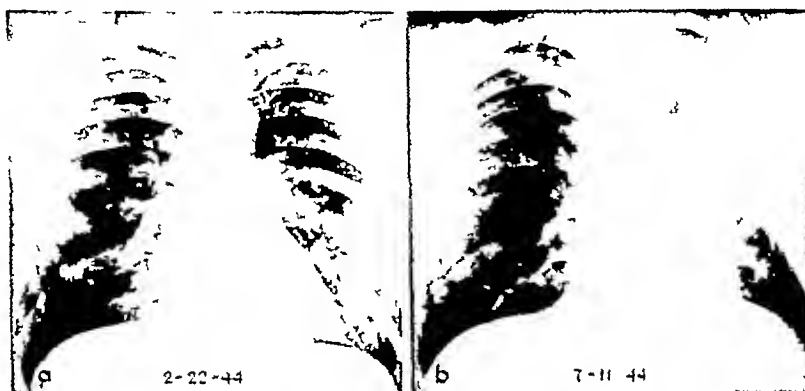


Fig 2 Case 2 Obstructive emphysema, left upper lobe, from bronchogenic carcinoma

a Postero anterior view Feb 22, 1944, in deep inspiration. The patient had no specific pulmonary symptoms at this time. There is a distinctly greater radiability in the left upper lobe. The left hilum shadow is increased in size.

b Re-examination five months later. Characteristic atelectasis of the left upper lobe is now shown. The root shadow on the left is much larger than previously. There is now a compensatory emphysema of the left lower lobe which has come to occupy the apex of the lung and can also be seen as an area of radiability medial to the collapsed upper lobe.

shown in this instance (Fig 2, b). This transition occurred somewhere between February and April of 1944. It appears to have been associated with a secondary infection since the patient actually had a pneumococcus Type 1 pneumonia involving the lower lobe as well as the atelectasis of the upper lobe.

CASE 3 A male, aged 49, was admitted to the University of Minnesota Hospital March 29, 1945. He had been suffering from a cough since 1920, which came on after an attack of influenza. He had experienced gradual weakness, loss of energy, shortness of breath, and a little pain in the left lower chest. He had lost about 20 pounds in the past five months. On Nov 20, 1944, the patient went to his family physician for the first time complaining of pain in the left chest and some cough. At that time a fluoroscopic examination of his chest was made by the physician and no definite abnormal findings were observed. The patient again consulted his physician

the lower lobe, and apparently some fluid in the pleural cavity. A tentative diagnosis of bronchogenic carcinoma was then made and the patient was sent to the University Hospital.

On entrance the physical examination showed evidences of considerable weight loss. There were retraction of the left chest on deep inspiration, dullness on percussion, and decreased breath sounds. Plain graphic study was made and a mass in the left lung root as well as obstruction of the left lower bronchus was clearly delineated (Fig 3, b). Bronchoscopic examination March 29, 1945, showed complete obstruction of the left lower lobe bronchus by a mass. Biopsy was done and the microscopic section showed squamous cell carcinoma. Exploratory surgery was performed April 20, 1945, but the mass was found to be too extensive for removal.

Comment The original film of the chest made Jan 8 (Fig 3, a) was considered negative, but on examination it gives clear evidences to indicate the presence of a carcinoma of the lung. There is emphy-

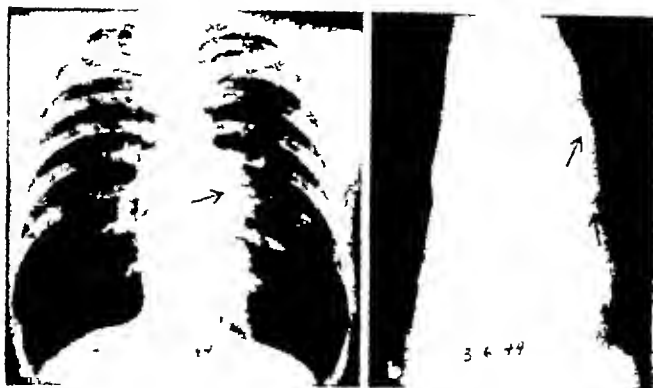


Fig 3 Case 3 Obstructive emphysema of left lower lobe from bronchogenic carcinoma

a Postero-anterior roentgenogram in deep inspiration made Jan 5 1944 Increased radiability of the left lower lobe is shown There is a marked enlargement of the left root shadow (arrow)

b Planigram made two months later The mass in the left hilum is more clearly outlined (lower arrow) and the high grade obstruction of the lower lobe bronchus is also shown (upper arrow)

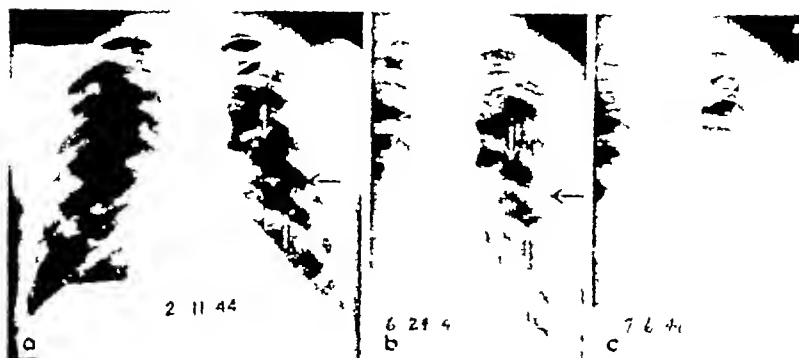


Fig 4 Case 4 Obstructive emphysema with bronchogenic carcinoma left

a Postero anterior roentgenogram in inspiration made Feb 11 1944 as a routine procedure The increased radiability in a local segment of the left upper lobe can be faintly made out (arrows) There is a ring like shadow just lateral to the root of the lung with a moderate area of increased density surrounding it The latter no doubt is due to the compressive atelectasis of the neighboring lung The left root shadow is somewhat increased in size

b Postero anterior roentgenogram made June 24 The left side only is shown The area of emphysema is still present (arrows) There is some beginning atelectasis in the lower lobe The enlarged root shadow is more apparent

c Postero anterior roentgenogram, left side only made July 6 Atelectasis is now present in the whole lower lobe and involving that portion of the upper lobe which was previously emphysematous The transition from emphysema to atelectasis is well shown here

sema of the left lower lobe and a fairly good-sized mass is present in the left hilum The increased radiability of the left lower lobe is difficult to delineate, since this man had a considerable emphysema of both lungs, related, no doubt, to a long-standing process, present for fifteen years Films in expiration at that time very likely would have accentuated the increased radi-

ability of the left lung and perhaps given a more distinctive clue to the diagnosis The change over from emphysema to atelectasis was well delineated in the various roentgenograms The demonstration of the mass in the mediastinum and the resulting obstruction of the bronchus was effectively made by means of planigraphy (Fig 3, b)

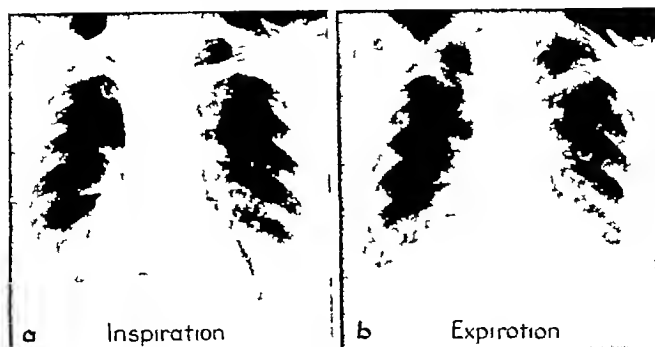


Fig 5 Case 5 Carcinoma right lower lobe bronchus, with obstructive emphysema and atelectasis

a Postero anterior roentgenogram in deep inspiration The lungs, heart, and diaphragm appear approximately normal except for an area of density at the right base in the cardiophrenic angle suggesting a local area of diminished aeration or atelectasis

b Postero-anterior roentgenogram in moderate expiration On the left the diaphragm has ascended in normal fashion, the heart being displaced somewhat to the left side The distinct difference in radiability between the right and left lungs is now shown the right lung being more radiable than normal in expiration The area of atelectasis remains the same The effect of inspiration and expiration in demonstrating the obstructive emphysema is well shown

CASE 4 A male, aged 66, was admitted to the Minneapolis General Hospital because of alcoholism and mental deterioration, June 28, 1944. He was suffering from weakness and some epigastric pain. He appeared dehydrated and malnourished. The sedimentation rate was elevated. There was a secondary anemia. The physical and laboratory findings were otherwise negative. A roentgen examination of the chest had been made upon a previous admission on Feb 11 (Fig 4, *a*) and thought to be negative. Re-examination of the film however, reveals a local area of increased radiability in the middle portion of the left lung with a slight zone of density around it. A second examination, June 24 (Fig 4, *b*), revealed a generalized increased radiability of the left lung denoting emphysema. Films were not made in expiration, but the emphysema is visible even in inspiration. About twelve days later a third examination (Fig 4, *c*) showed a massive atelectasis of the left lower lobe indicating the conversion of a partial obstruction to a complete obstruction. The patient gradually became weaker and died.

Autopsy revealed a bronchogenic carcinoma filling the left main bronchus but obviously originating in the left lower lobe.

Comment Here again, earlier recognition of the process might have occurred if a film had been made in expiration so that the emphysema would have been more apparent. The rapid change over from emphysema to atelectasis is well demonstrated.

CASE 5 A female, aged 69, was first seen on Dec. 15, 1945. For about twelve months previously she had had a dry, irritating cough with some stridor. At various times she had also experienced hoarseness, dyspnea on exertion, and mild orthopnea. She had lost about 20 pounds during the past year and a half. There were no other symptoms. On physical examination the respiration had a stridorous quality. There were some respiratory lag, dullness and impaired breath and voice sounds on the right side. Wheezing rhonchi were heard over the right lung. Occasionally the cough was productive. On fluoroscopic examination there was found a distinct diminution in the movement of the diaphragm on the right side, which remained low during expiration, while the left diaphragm elevated itself. Clear-cut signs of emphysema in the right upper area could be made out, and some evidences of atelectasis or decreased aeration in the right lower. Films confirmed this finding (Fig 5, *a* and 5, *b*). Planigrams were then made and a defect in the right main bronchus arising apparently 2 cm from the carina could be made out. This appeared to occlude the lower lobe bronchus almost completely but only partially obstructed the upper lobe. The possibility of a benign tumor was then considered. Bronchoscopy was done Dec 21, and bronchography at the same time. An ulcerating lesion could be made out bronchoscopically at the carina, extending down the right main bronchus. The orifices of the right upper and middle lobe bronchi appeared open, although the ulceration extended down toward these areas. Granulomatous lesions, however, reduced the lumen of the right main bronchus to approximately one half its norm. These granulomatous

lesions extended down into the orifice of the lower lobe bronchus and almost completely occluded it. There was, however, still some opening in the lumen of the right lower lobe bronchus. On bronchography a defect in the lower lobe bronchus could be clearly made out just at its bifurcation. There seemed to be some compression of the lumen of the upper lobe bronchus and the main stem bronchus apparently from an extrinsic mass. Biopsy of the granulomatous material showed a typical bronchiogenic carcinoma of the small cell type.

main bronchus producing emphysema, with almost complete obstruction of the right lower lobe bronchus producing marked decrease in aeration. The findings were first observed during routine fluoroscopy of the chest, although the symptoms pointed somewhat in this direction.

Two other cases should be added to this category although they will not be de-

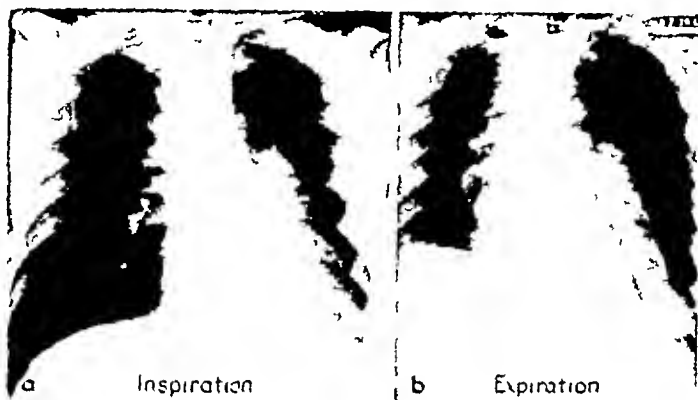


Fig. 6. Carcinoma of the left main bronchus with atelectasis of lower lobe and emphysema of upper lobe. Case of Dr. T. M. Berman, Miami Beach, Florida.

a. Anteroposterior roentgenogram, supine position in deep inspiration. Increased density of the heart on the left side and density extending beyond it indicate an atelectasis of the lower lobe, as well as a tumor in the lung root. There is a moderate increase in radiability in the left upper lobe, the difference between the two lungs being apparent even during inspiration. Note the mass of enlarged lymph nodes in the right perihilar area.

b. Anteroposterior roentgenogram, supine position in deep expiration. The diaphragm has ascended on the right. The radiability of the right lung has diminished, as is normal in expiration. The heart is displaced sharply to the right side. The atelectatic left lower lobe is exposed by the displacement of the heart. The much greater radiability of the left upper lobe as compared to the right is clearly apparent, indicating the obstructive emphysema of the upper lobe, which was due to partial obstruction of the left upper lobe bronchus. The atelectasis of the lower lobe was due to complete obstruction of this bronchus by the same carcinoma. The effect of inspiration and expiration in demonstrating the findings in the lungs is well brought out.

Because the ulceration extended up into the carina, surgery was not done. Some radiation was given with apparently some relief temporarily. An acute episode later developed, possibly related to the irradiation. Since then the patient has been lost sight of.

Comment. In this case the x-ray findings are relatively minimal except for the obstructive emphysema of the right lung, which is combined with some beginning atelectasis of the lower lobe. Thus we have the partial obstruction of the right

scribed in detail. One of the patients is a miner who was being examined annually because of the possibility of silicosis. On the last routine examination, made a little over a year before his entrance into the University Hospital, restudy of the films showed a distinct emphysema of the right upper lobe. This film was made in deep inspiration and the findings are so slight that it is not possible to reproduce them, but we were satisfied on independent examination that actual emphysema existed

at that time When the patient came to the hospital, evidences of atelectasis were already present and a definite obstructive tumor of the right upper lobe bronchus was made out both by bronchography and planigraphy This proved to be a bronchogenic carcinoma

A final case likewise will not be described in detail We are indebted to Dr T M Berman of Miami Beach, Florida, for the privilege of reporting it The patient was proved to have bronchogenic carcinoma on the left side, the tumor producing emphysema and atelectasis in the same lung simultaneously The inspiratory roentgenogram (Fig 6, *a*) shows extensive density in the left lower lobe, representing an atelectasis of considerable degree The aeration of the left lung above this and of the right lung appears almost equal, there may perhaps be a slight degree of increased radiability on the left side A roentgenogram in expiration (Fig 6, *b*), however, is very illuminating While the atelectasis in the lower lobe remains about the same, the upper lobe appears far more radiable than the opposite lung The mediastinum has moved well over to the right side and the right diaphragm is elevated The left remains the same This is typical of an obstructive emphysema and in this case was due to a tumor which completely occluded the lower lobe bronchus and protruded sufficiently into the lumen of the upper lobe bronchus to produce a partial obstruction with obstructive emphysema in the phase of expiration

The value of the roentgenogram in expiration is again delineated in these two cases In the first the diagnosis might have been suspected a year before it was made if an expiratory film had been made In the last case the striking difference in the appearance of the emphysematous lobe in inspiration and expiration is well brought out (Fig 6)

SUMMARY AND CONCLUSIONS

Obstructive emphysema is an early sign of bronchogenic carcinoma resulting from partial obstruction of a bronchus by the tumor

It is best demonstrated by roentgenograms or fluoroscopic examination made during expiration The transition from emphysema to atelectasis as the tumor grows and completely obstructs the bronchus may be readily determined by repeated roentgen examination

Five cases are reported in detail and two partially to illustrate the importance of these observations

Patients suspected of bronchogenic carcinoma but without frank roentgen findings should always be examined in expiration as well as inspiration

Careful study should be given to minor differences in radiability of the two lungs to determine whether obstructive emphysema is present Such a finding should lead to further investigation by bronchography, planigraphy, and bronchoscopy

University of Minnesota
Minneapolis 14 Minn

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SUMARIO

Enfisema Signo Roentgenológico Temprano del Carcinoma Broncígeno

El enfisema obstructivo constituye un signo temprano del carcinoma broncígeno, ocasionado por la obstrucción parcial de un bronquio por el tumor. Se observa mejor en los roentgenogramas o exámenes roentgenoscópicos ejecutados durante la espiración. Por medio de exámenes roentgenológicos repetidos puede determinarse fácilmente la transición del enfisema a la atelectasia a medida que el tumor crece y obstruye completamente el bronquio. Describense cinco casos minuciosamente y dos

parcialmente para demostrar la importancia de estas observaciones.

A los pacientes en que se sospecha carcinoma broncígeno y los hallazgos radiológicos no son terminantes, debe examinárseles siempre durante la espiración así como la inspiración. A fin de determinar si existe enfisema obstructivo, hay que estudiar cuidadosamente las pequeñas diferencias en radiabilidad de los dos pulmones. Un hallazgo de esa naturaleza debe instigar nuevas investigaciones broncográficas, plamigráficas, y broncoscópicas.



Roentgenologic Study of the Small Intestine

I Neoplastic and Inflammatory Diseases¹

FRED J HODGES, M.D., R WAYNE RUNDLES, M.D.², and JOSEPH HANELIN, M.D.

NO PHYSICIAN can long engage in the practice of medicine without becoming impressed by the fact that complaints variously related to the alimentary tract are commonplace and diverse. More often than not, when radiologic consultation is arranged, no convincing explanation for the patient's symptoms is manifest at the fluoroscope or in supplementary roentgenograms. It has been the uniform experience of many radiologic groups who examine large numbers of persons each year, in search of demonstrable signs of gastro-intestinal disease, that dependable x-ray evidence of significant abnormality is to be expected in no more than 25 to 30 per cent of all patients whose digestive complaints have brought them to the radiologist for diagnostic consultation. In most of the cases where no abnormality can be found, the presenting symptoms are of such a nature that it is sufficient for the radiologic examination merely to exclude unlikely lesions. In other cases, however, there may be persistent, annoying, and even incapacitating symptoms arising from abnormalities which routine procedures may fail to uncover. Negative reports from the roentgenologist often result in lost opportunities for therapy. Harm may follow the all too frequent impeachment of the patient's psychiatric integrity.

Gross pathologic lesions of the esophagus, the stomach, and the colon are recognizable with a high degree of accuracy by able roentgenologists with or without the advantage of leading clinical information. In other words, if digestive tract symptoms are produced by such lesions as peptic ulcer, gastric or colonic neoplasms, ulcerative colitis, and the like, recognition and

accurate diagnosis of the underlying cause of the patient's complaints may be anticipated with reasonable confidence on the basis of x-ray findings. Disorders of the small intestine, on the other hand, producing motor or absorptive disturbances, will be as consistently overlooked unless clinical acumen is exercised and diagnostic efforts are properly directed.

Ordinarily employed procedures in the roentgenologic search for alimentary tract disease are centered to an overwhelming degree upon the proximal three feet and the distal five feet of the tube, those portions which experience has taught harbor the great bulk of x-ray recognizable abnormalities. By and large, the longest portion of the gastro-intestinal tract, beginning at about the ligament of Treitz and extending to a point within 12 to 18 inches of the cecal junction, is scrutinized, if at all, in a most desultory fashion by most of us who are engaged in gastro-intestinal diagnosis. It is necessary to bear in mind that, despite its many and spectacular achievements as a demonstrator of disease processes, the x-ray approach to diagnosis is by no means omnipotent. Dependent, as he most certainly is, on the observation of form and motion of the gut wall, the roentgenologist—and the physicians who call him in consultation—must remember that a great many deviations from normal can exist which do not produce roentgenologically recognizable signs. It is thoroughly possible and entirely probable, on the other hand, that mild and grave disorders not now recognized can be readily discovered by increasing the scope and versatility of gastro-intestinal x-ray diagnostic procedures.

¹ From the Departments of Roentgenology and Internal Medicine, University Hospital, University of Michigan, Ann Arbor. Read by title at the Thirty first Annual Meeting of the Radiological Society of North America, Chicago III, Nov. 9-10, 1945. Submitted for publication in April 1947.

² Since July 1, 1945, attached to the Department of Medicine, Duke University School of Medicine, Durham, N. C.

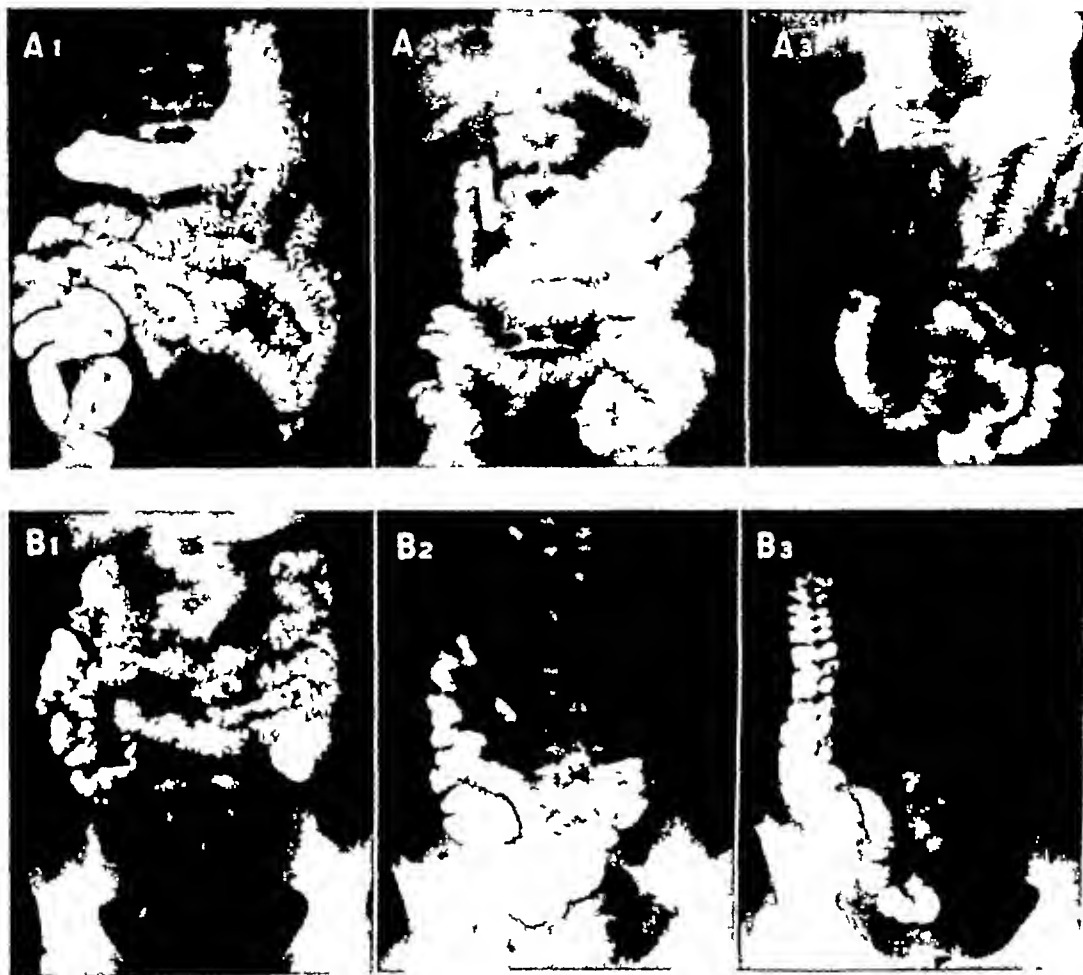


Fig 1 Normal small bowel behavior

A 1 2 3 Typically normal appearance of upper small intestine immediately after barium feeding in three different patients

B 1 2 3 Normal behavior of small intestine as observed in the same patient immediately, two and a half and five hours after barium ingestion

The technical steps employed in the examination of the gastro-intestinal tract vary widely in the matter of detail as practised in various clinics, offices, and hospitals throughout this country. In general, however, the great majority of all x-ray examinations of the intestinal tract involve one or the other or both of two basic procedures. The first of these involves the administration of a suspension of inert opaque salts by mouth, whereas the second depends upon the injection of a similar opaque mass per rectum. The proportionate emphasis upon fluoroscopy and radiography in making observations upon the

gut when so prepared, as well as the time and the distance of travel over which the progress of injected material is followed, differs greatly in the hands of various examiners (8, 34).

Generally speaking, the major extent of the small intestine receives scant attention in the course of most gastro-intestinal examinations. Oftentimes more or less perfunctory filming at frequent and arbitrary intervals is followed almost religiously with major attention on the possible role of the appendix in producing obscure symptoms. Not until relatively recent years have radiologists made serious attempts to glean

significant diagnostic evidence regarding the status of the small intestine from the jejunum to the low ileum. One method which has gained some favor, the small bowel enema, has been advocated by Schatzki (29). This method, undoubtedly useful in some situations, is not without its practical disadvantages. Cole (5), Pendergrass *et al* (26), Golden (8, 9, 10, 11, 20), Mackie, *et al* (22, 23, 24), Snell and Camp (31), to mention but a few names, have been pioneers in this country in the matter of directing roentgenologic attention to the small intestine. As the result of the interest and industry of these workers, much has been learned regarding the anatomical and physiological features of the small intestine as demonstrable by x-ray methods, and as a logical consequence the general fund of knowledge regarding disease states involving the small bowel has been considerably expanded. Alterations in the behavior of the small intestine, as well as often overlooked details of appearance, have been described following the chemical and physical alteration of the contrast material used (26). These observations, if they have done nothing else, have called attention to the fact that the small intestine is capable of reflecting responses to environment and stimulation. It seems logical that, with the accumulation of more experience in this field, roentgenologists will one day come to recognize with confidence many other factors which can visibly alter the form and behavior of the small intestine.

Excursions into this relatively new field of roentgenological interest have stimulated renewed interest in the histology, the neuro-anatomy, and the physiology of the intestine (11). Much attention is being paid to the intimate pattern imparted to opaque material within the lumen by the folds of the mucosal lining. While the nervous and muscular mechanisms responsible for small bowel behavior are as yet insufficiently well established to permit uniformity of opinion by all interested investigators, there is good reason to believe that the mucosal pattern is dependent upon

the activity of the muscularis mucosae, which is capable of operating independently of the circular and longitudinal muscular coats. It can be shown, for example, that the direction of mucosal folds is independent of lumen caliber (11) and that the direction of folds may change with great rapidity from transverse to longitudinal in immediately neighboring segments of gut. Several examples of normal small bowel appearance are illustrated in Figure 1, notable among these features being the sharp, delicate fold imprints seen in the duodenum and upper jejunum, the uniformity of lumen width, and the transition to a blunter or coarser mucosal pattern when the barium column reaches the ileum. It is to be remembered that range of variability in the matter of small bowel appearance is considerable. In Figure 2, profound changes in the appearance of mucosal pattern are shown under various conditions. In the present state of our knowledge at least, it does not seem wise to attach too much significance to minor or controversial alterations in appearance unless supported by other clear-cut evidence of disease.

Grosser methods of evaluating the status of the small intestine relate to over-all accomplishment as measured in broad terms of transit time, as well as emptying time of the stomach (which is capable of materially affecting the time of transit through the small bowel), absolute and relative caliber dimensions, and the scattering or breaking up of the opaque column into bowel segments of varying length and configuration. The term "puddling" enjoys rather wide usage in describing an appearance, considered to be abnormal, which is characterized by somewhat widely separated deposits of barium in isolated segments of small bowel.

When the sole evidence of gastro-intestinal abnormality in a given instance is found to depend upon alterations in behavior of alimentary tract structures, the disturbance may fairly be spoken of as functional without implying that it is psychogenic. It is our habit to disregard or



Fig 2 Normal small bowel behavior
 A Characteristic upper small bowel mucosal pattern. Note changeability of mucosal folds—horizontal and longitudinal folds seen in immediately adjacent segments of gut.
 B-1, 2 Normally changeable appearance of mucosal pattern in terminal ileum as seen following barium enema before and after voluntary evacuation.
 C 1, 2 Normal variability of terminal small bowel appearance as seen five hours after barium ingestion and on another occasion following barium enema.

minimize roentgen signs of alimentary tract dysfunction when they are over-shadowed by palpable evidences of intrinsic organic disease. More or less by common consent, the term "functional disorder," at least when the condition is discovered on the basis of x-ray findings, implies that the reasons for faulty function are not immediately apparent roentgenographically. Some organic lesions which may not be recognized with conviction in their own right are apprehended on the basis of fairly well localized and striking changes in function. It is only when we are at a loss for objective evidence which points directly to a morphologic lesion that we fall back upon the word "functional" in our roentgenologic jargon.

METHOD OF STUDY

Many of the technics which have been devised to subject the small intestine to exhaustive scrutiny are so time-consuming as to be prohibitive when it is desirable to examine large groups of patients. Without wishing to be critical of the diagnostic merits of such procedures, one might well point out that less exacting technics may be used for screening purposes to locate likely candidates for more exhaustive studies. One such screening method enjoys the advantage of great simplicity and facility of application while yielding a considerable amount of valuable information. This screening method virtually eliminates fluoroscopy, which makes the greatest time demand, by restricting the latter to the time of barium feeding and the few moments required to observe the progress of the meal well into the jejunum. In addition to this brief fluoroscopic observation, the method employs full abdomen filming in the form of single exposures immediately at the completion of the fluoroscopic examination, and repeated at a few specified intervals thereafter. Intervals of one hour, two and a half hours, and five hours have been found to provide a great deal of information regarding the status of the small bowel. Figure 1 (B-1, 2, 3) represents films made immediately and at two and one

half and five hours after feeding in the case of one of 12 healthy individuals studied. It is not to be understood that the particular distribution of barium shown in this illustration is dependable within narrow limits as an expression of the normal. Every radiologist of experience is well aware that variability rather than constancy is the rule in all forms of gastrointestinal radiography. Within limits, however, one is entitled to expect that a normal stomach will be virtually empty at two and one half hours and that the barium which has passed the pylorus will have progressed far into the ileum. He may further expect that at five hours filling of the right colon will be well advanced, and that barium remaining in the small bowel will be confined to the terminal portion of the ileum. While exceptions to the rule are numerous, it is common to observe that all of the barium administered will be found below the level of the umbilicus and to the right of the mid-line at the five-hour interval. Organic lesions which obstruct the small bowel lumen at any level will profoundly disturb this time-table, and abnormalities, whatever their nature, which disrupt the orderly mechanism of propagation of the meal will be apprehended. Organic lesions or functional disturbances capable of modifying the consistency of the gut wall or the continuity of muscular activity in any of the coats will be very apt to come to light in either or both of the standardized exposures at two and one half and five hours.

This plan of roentgen examination was used in the study of more than 100 patients selected on the basis of having symptoms thought to represent small bowel dysfunction. These symptoms comprised, in general, gross abnormalities of bowel habit, chronic diarrhea or acute refractory constipation not due to demonstrable colonic disease, abdominal pain of colicky nature unrelated to bowel movements, gaseous distention, borborygmi, and severe anorexia sometimes with nausea and vomiting. A few patients had had in addition repeated unexplained hemorrhages from the

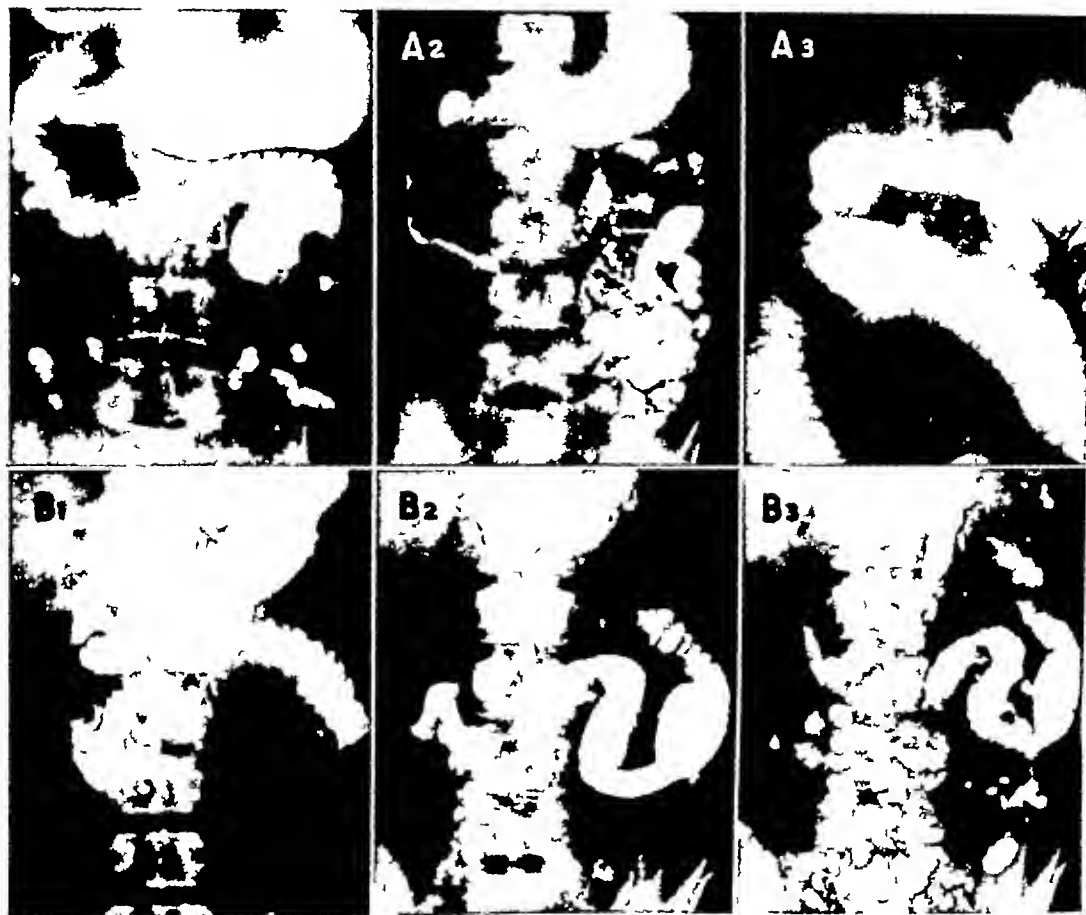


Fig 3 Organic lesions involving small bowel

A 1 Case 1 Primary adenocarcinoma of jejunum producing high grade obstruction 2 Case 2 Lymphoblastoma involving the duodenum 3 Case 3 Primary carcinoma low in the jejunum producing generalized distention of proximal small bowel Note preservation of distinct mucosal folds

B 1, 2, 3 Case 4 Regional ileitis involving a considerable segment of jejunum Note delayed emptying of smoothly margined convoluted loop of bowel in mid abdomen which remains filled two and a half and five hours after barium feeding

intestinal tract or chronic anemia due to blood loss or absorptive abnormality. The final diagnoses included chronic ileojejunitis, severe vitamin B deficiency, neuropathies involving the autonomic nerves, and alteration in appearance following sympathectomy and other surgical procedures.

Once roentgenologic findings indicative of structural abnormality or functional misbehavior of the small intestine are uncovered, the difficult problem of interpretation arises. Many diseases and processes have to be considered in differential diagnosis, and final conclusions are seldom possible from roentgen study alone. Neo-

plasms of the small intestine, which are fortunately rare, give rise to characteristic signs only after the lumen has been considerably deformed, often to the point of obstruction (35). Chronic inflammatory disease of the small intestine, occurring with hepatitis (11, 12, 21, 25), ulcerative colitis (24), and sometimes in a form progressing to regional cicatrization (4, 6, 7, 17, 18, 30, 32, 33), may or may not be distinguishable roentgenologically from non-inflammatory lesions. The function and appearance of the gut may be altered by edema consequent to portal vein hypertension or obstruction, low serum proteins (1, 2, 11), severe anemia (16), hookworm

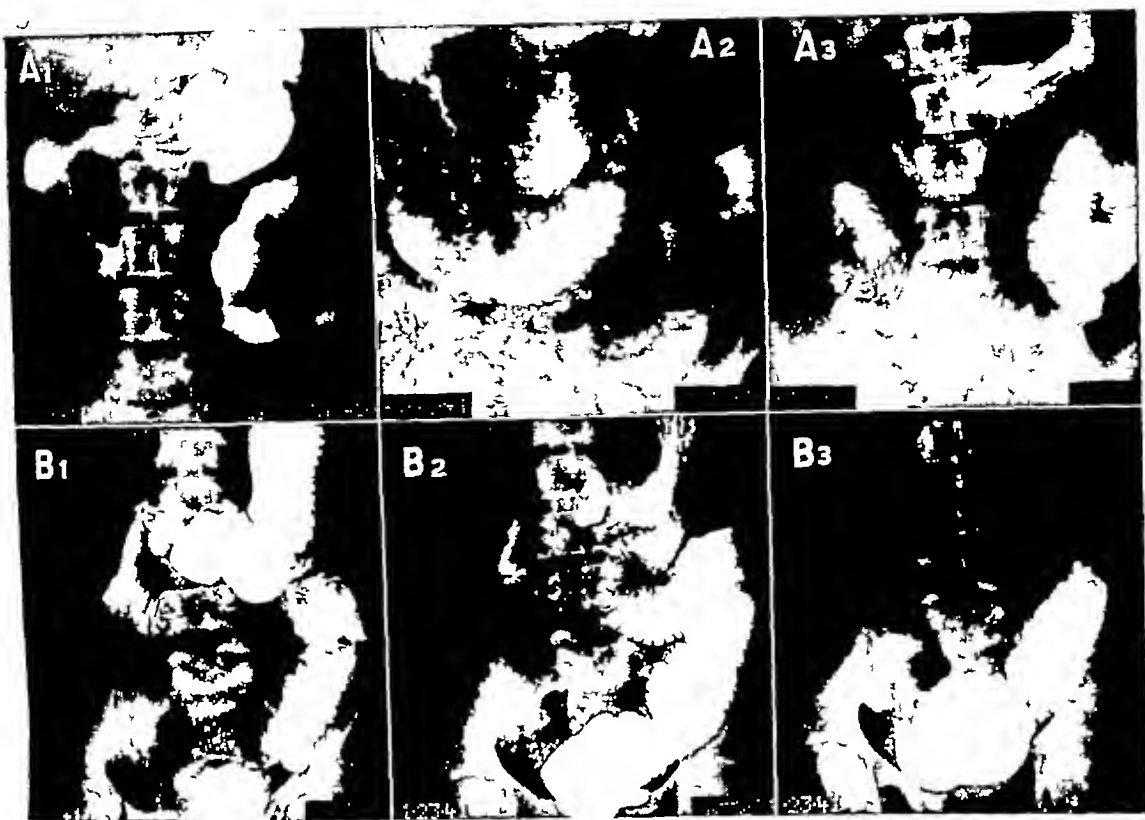


Fig 4 Organic lesions involving small bowel extensive regional enteritis involving jejunum

A Case 5 Note the profound deformity of a loop of jejunum to the left immediately after barium feeding (A-1) with widening of lumen and loss of normal mucosal markings. At two and a half hours (A-2) a horizontal segment of jejunum at a lower level can also be seen in which the lumen is broadened and the mucosal pattern is coarse and irregular. Twenty months later (A 3) the only residual signs of previous inflammatory disease are slight widening of the lumen and slight coarsening and irregularity of mucosal folds.

B 1, 2, 3 Case 6 Regional enteritis 3 feet distal to the duodenal jejunal junction producing complete obstruction as shown immediately, two and a half and five hours after barium feeding.

infestation (15, 19), in Henoch's purpura (36), and perhaps in allergic conditions with urticaria (11). A generalized disease of the connective tissue of the body, scleroderma, may involve the intestinal wall (13). Gross abnormalities of the intestinal tract have been attributed to diseases of nutrition, vitamin B deficiency, and sprue (10, 20, 22). It is often a question as to whether the nutritional deficiencies are primary or actually the result of another disease (3). Finally, intestinal dysfunction has been attributed to disturbances of the intrinsic and extrinsic autonomic nerves (11, 27, 28). Too little evidence has been accumulated regarding all of these factors to allow more than a rough estimate of the expected roentgen abnormalities in interpreting a given case.

In postulating the existence of neoplastic or inflammatory lesions of the small intestine the roentgenologist in general depends upon fixed or relatively fixed deformities of the gut lumen, displacement of the gut segments, and signs of luminal obstruction. Several small bowel lesions of proved identity are illustrated in Figure 3. In the first of these (A-1) an annular adenocarcinoma in the proximal jejunum had produced high-grade luminal obstruction with consequent dilatation proximal to the obstruction site. A lymphosarcoma involving the major portion of the duodenum (A-2) was recognizable as an organic lesion on the basis of profound and extensive deformity of the gut segment as well as displacement of the affected and uninvolved gut loops. Again generalized distention,

without obliteration of normal mucosal folds, throughout a considerable length of small bowel proximal to an obstruction point led to the correct diagnosis of a primary carcinoma of the jejunum 3 feet beyond the ligament of Treitz (Fig 3, A-3). In the case of a fourth patient (Fig 3, B-1, 2, 3), more extensive organic disease involving several inches of jejunum in mid abdomen, slightly to the left of the midline, obliterated normal mucosal markings, rendered the affected segment of gut relatively non-phable, and partially obstructed the transit of barium. In all of these situations, localized organic small bowel disease was reported with confidence on the basis of objective evidence.

The situation shown in Figure 4 (A-1, 2, 3) represents chronic regional enteritis, again involving the jejunum. This patient was examined during a period when acute symptoms were present and eighteen months later during quiescence. Here again the roentgenologic signs of intrinsic deformity, as well as partial obstruction to the transit of barium, were clear-cut and were accepted as reliable evidences of organic disease. The fact that spontaneous recovery did not occur without some tell-tale residual evidences of disease is nicely shown in A-3, in which slight residual widening of lumen and a slight coarsening of mucosal pattern were seen to persist. Interpretation of the disease process on the basis of the second roentgen study alone would have been difficult. Case 6, illustrated in Figure 4 (B-1, 2, 3), is an example of regional enteritis in which the organic deformity of the affected segment cannot be seen because associated obstruction is profound. In this instance the presence of the lesion was postulated on the basis of obstruction and its non-neoplastic character was assumed because the clean-cut overhanging edges of gut so typical of annular neoplasm were not to be seen.

Additional examples of organic small bowel lesions which advertised their presence by producing demonstrable roentgenologic signs which may be considered to be diagnostic are shown in Figure 5. Per-

sistent irregular deformity and associated displacement of the extreme terminal ileum shown in A-1 represent the effect produced upon neighboring small bowel by an appendiceal abscess. Loss of all mucosal markings, irregularity of lumen width, and rigidity of walls as proved by multiple exposures mark A-2 as an example of ileocolitis of the ulcerative type. What may be considered an almost classical deformity of ileocecal tuberculosis is shown in A-3.

Case 10, shown in Figure 5 (B-1, 2), represents disease which involves a larger segment of the small intestine. Here delayed transit, variability of lumen width, and widespread modification of mucosal pattern were produced by extensive regional enteritis. A roentgenogram of the surgical specimen from this case is shown in B-3. This specimen is interesting because it shows, at the lower margin of the illustration, multiple zones of contracture of the lumen ending abruptly at a point where the gut lumen has been expanded as the result of the over-all obstruction. It is interesting to ponder whether long-standing regional ileitis produces "up-stream" changes simply by obstruction or whether the inflammation has actually been more extensive and led to scarring with damage of the muscles and nerves of the gut wall.

To discover such striking abnormalities with any degree of frequency among patients referred for roentgen study of the small intestine is certainly not to be expected. Among patients carefully selected for such study obviously disturbed function will be found in less than one-half. In relatively few of these will the roentgen findings justify any presumption as to the nature of the underlying disease. In 11 cases, which have been neither abstracted nor illustrated here, no entirely convincing roentgen sign could be found to indicate that the disorder was certainly of inflammatory origin. In every instance, however, there was overwhelming clinical or surgical evidence of chronic non-obstructive ileojejunitis. In 2 there was in addition associated chronic ulcerative colitis. The roentgenologist can only re-

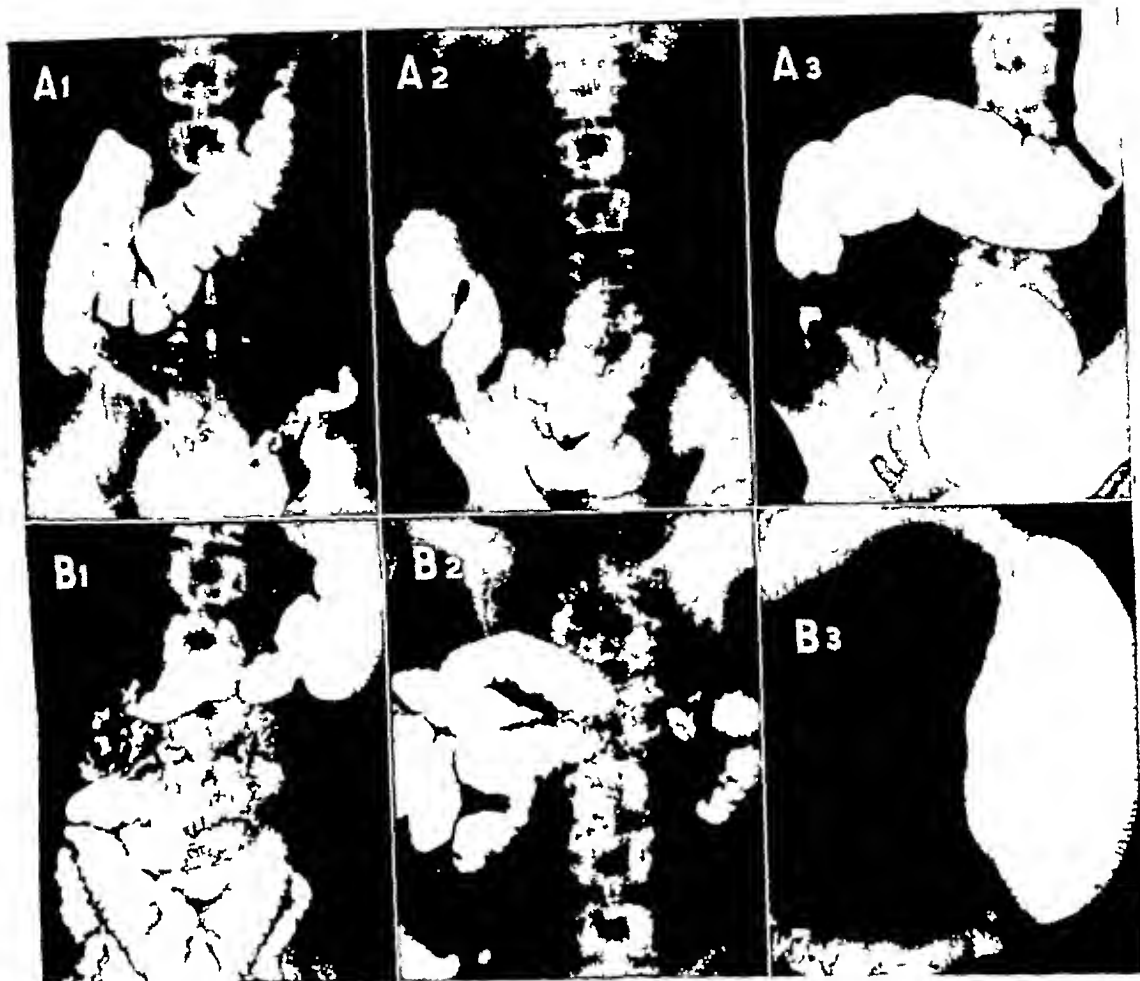


Fig 5 Organic lesions involving small bowel

A 1 Case 7 Narrowing irregularity of lumen slight upward displacement, and appearance of rigidity involving the terminal ileum produced by periappendiceal abscess

A 2 Case 8 Segmental narrowing and dilatation of terminal small bowel, tapered ileocecal junction, and contracted cecal tip in a patient with proved ulcerative ileocolitis

A-3 Case 9 Characteristic profound deformity of the extreme tip of the cecum, narrowing of the ileocecal junction, and intense narrowing of the terminal ileum, with loss of all mucosal pattern, in a patient with ileocecal tuberculosis

B 1 2 Case 10 These exposures immediately and five hours after barium feeding show extensive disturbance of the mucosal pattern and great delay in transit in the case of a patient with extensive regional enteritis involving the lower ileum

B 3 Case 10 Roentgenogram of operative specimen obtained ten months later Note greatly dilated segment distal to smoothly narrowed portion and multiple strictures in the generally contracted distal segment at the lower left corner of the illustration

port in such instances that there is reliable evidence of "dysfunction" and allow clinical or pathologic studies to establish the etiology

Roentgenograms from the records of two patients are presented for the purpose of illustrating to what profound degree the ordinary functional activities of the intestinal tract can be disrupted In spite of all possible study, the cause of the difficulty in these cases could not be ascertained

In Figure 6 are reproduced selected roentgenograms of a patient (Case 11) whose clinical situation was replete with striking evidence of generalized disturbance of the intestinal neuromusculature Even casual inspection of the illustrative material indicates that the entire alimentary tract from the esophagus to the pelvic colon is behaving in a most peculiar manner Cardiospasm, shown in the first illustration (A-1), was the initial reason for roentgen examina-

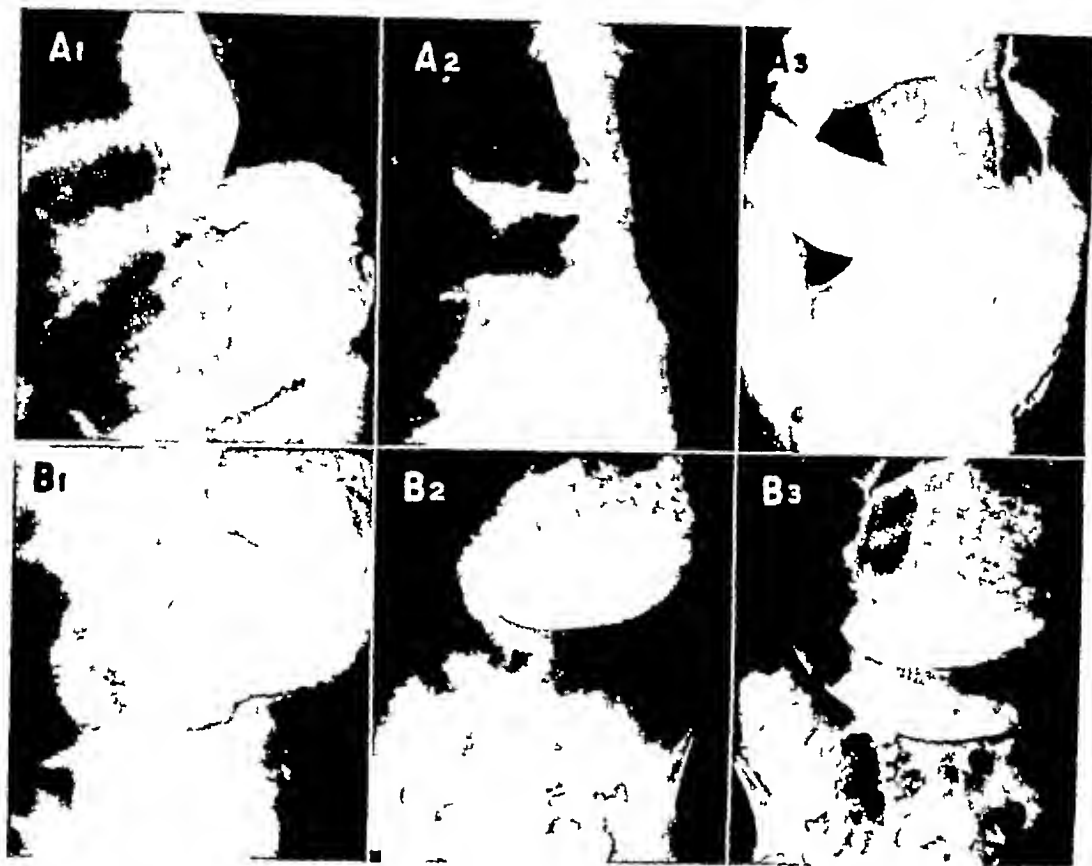


Fig 6. Functional small bowel disturbance

A 1, 2, 3 Case 11. Cardiospasm greatly distended small bowel and colon (patient standing) and the colon following barium enema showing greatly increased capacity, generalized loss of tone, and absence of typical haustral markings in the transverse portion.

B 1, 2, 3 Case 11. Exposures immediately, five and twenty-four hours after barium feeding indicate the degree of delayed gastric emptying encountered in this patient as well as profound delay in small bowel transit time and widespread loss of tone.

tion. That this was a minor expression of the profound disturbance affecting the entire alimentary tube is well shown in the remainder of the illustrations (A-2, 3, B-1, 2, 3). There seems to be ample evidence to indicate that the complex and elaborate nervous and muscular mechanism which controls and co-ordinates the motor function in the intestine was extensively disrupted.

Case 12 (Figs 7 and 8) in this series shows an exceptionally severe disturbance in the function of the entire gastro-intestinal tract similar to Case 11. The patient was studied and treated intensively for a period of eight months. At no time was there clinical evidence of specific vitamin

deficiency, anemia, or neurologic disease involving the cerebral, spinal, or autonomic nerves. There was no significant response to therapy and death eventually occurred, as a result of failure of the motor and absorptive functions of the intestinal tract. At necropsy there was extreme atrophy of all the organs, malnutrition, and muscular atrophy with diffuse fibrosis of the entire intestinal tract. Special examination of the central and peripheral nervous system, while unfortunately limited to small portions of these structures, nevertheless demonstrated profound change. Marchi preparations of the spinal cord and sciatic nerve showed advanced myelin degeneration (Fig 7, B-3, Fig 8, A). The myelin

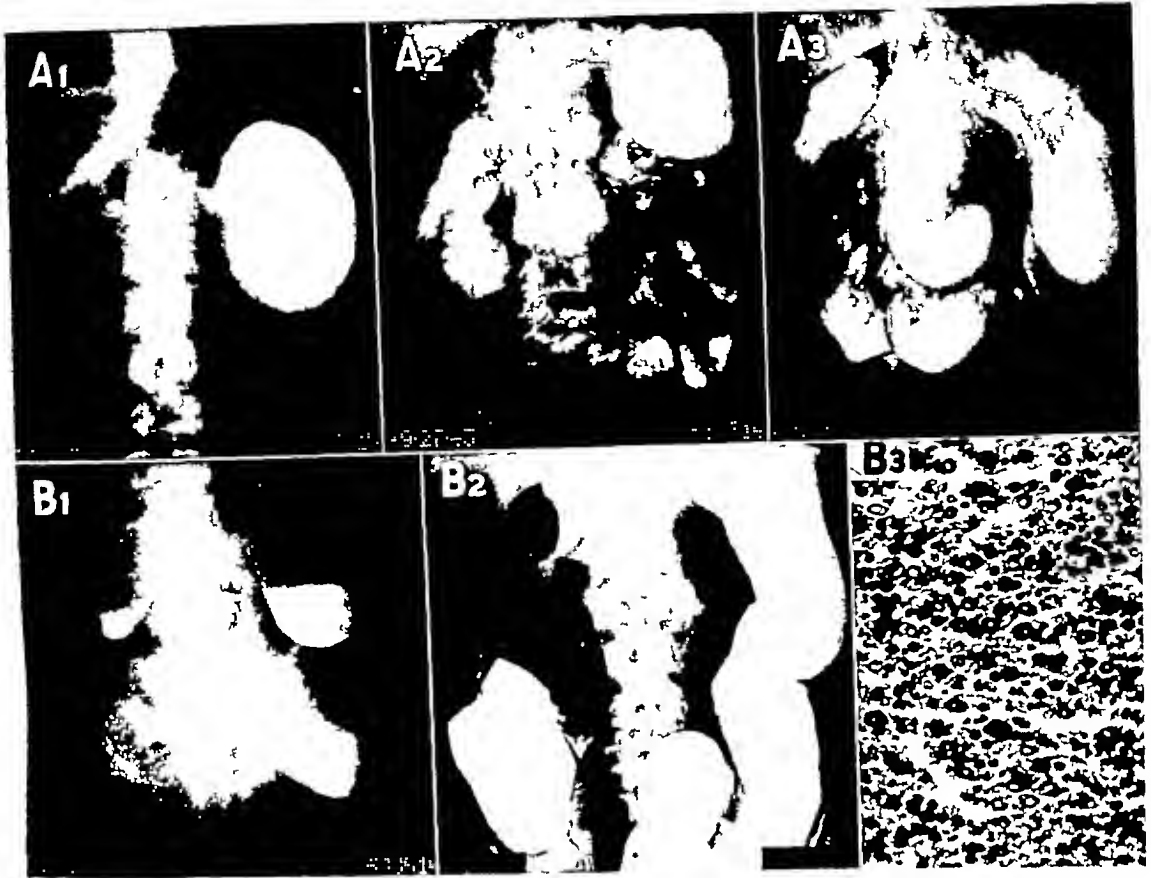


Fig 7 Functional small bowel disturbance

A 1 2 3 Case 12 Appearance of small bowel and stomach immediately and at two and a half and five hours after barium feeding. Observe tremendously delayed small bowel transit time delayed gastric emptying, and gas accumulation in small bowel and colon

B 1 Case 12 Film made in standing position same patient five hours after barium feeding, six weeks after initial examination. B 2 Voluminous atonic colon same patient four months later. B 3 High power photomicrograph showing advanced degeneration of the white matter of the spinal cord with edematous swollen, and disintegrating myelin sheaths stained black with osmic acid Marchi technic (Apochromat Bausch and Lomb 83 mm ampliplan low)

appeared swollen and broken into numerous fragments which stained jet black with osmic acid. The intramural nervous system of the intestinal tract could only be examined by ordinary staining methods. The ganglia of Auerbach's plexus, as shown in a van Gieson preparation (Fig 8, B) were swollen, their neurones were reduced in number, and the perisomatic glia was proliferated. Nerve fibers connecting ganglia exhibited degeneration comparable in severity to that of the sciatic nerve. Because of the limited amount of nervous material studied, interpretation of the histopathologic findings must be made with reserve. It is evident, however, that

both the central and peripheral nervous system suffered damage to a degree which was no longer compatible with life. The profound functional disturbance of the intestinal tract as demonstrated roentgenographically appears to be intimately related to the intramural nervous system changes. A satisfactory explanation of the whole course of this patient's illness is not forthcoming. The neurologic changes are particularly engrossing and challenging. At this time one cannot be certain whether they were primary in origin, or secondary to some systemic disorder. Their severity, however, underlines their significance. Intensive study of the peripheral and central

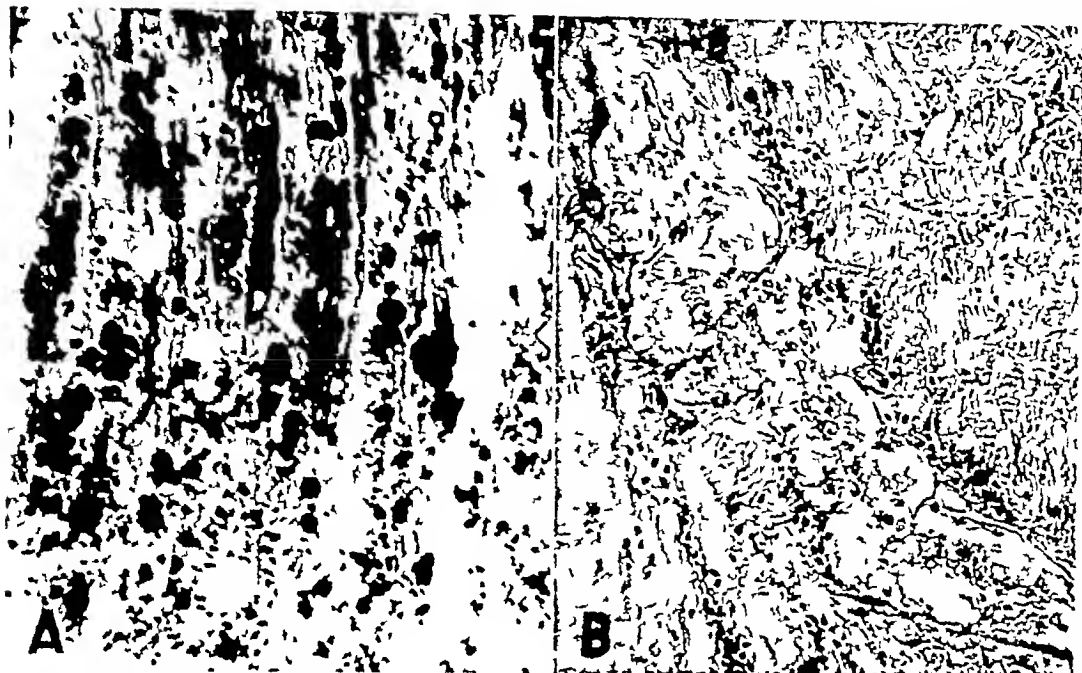


Fig 6 Case 12 A Photomicrograph showing advanced degeneration of the sciatic nerve with numerous coarse globules of destroyed myelin stained black by Marchi technique (Lens combination as in Fig 7)
 B Ganglion of Auerbach's plexus showing edema, advanced degeneration of the neurons and proliferation of the perineurial glia (Lens combination as in Fig 7)

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CASE HISTORIES

CASE 1 C A, a 60 year-old telephone line foreman, experienced, about six months before his hospital admission, pain in the upper left side of the abdomen and vomiting of recently eaten food which was sometimes bile stained. Finally he could retain only small amounts of liquid food and lost some 45 pounds in weight. The physical examination dis-

closed a hard mass, the size of a lemon in the left upper quadrant. The only abnormal laboratory finding was a hemoglobin of 68 per cent. X-ray examination of the intestinal tract demonstrated an annular constricting lesion of the proximal jejunum (Fig 3 A 1). At operation the first 10 centimeters of the jejunum were found to be dilated and thickened above an annular constricting lesion. Resection was carried out and pathologic examination showed a Grade III adenocarcinoma arising in a papilloma.

CASE 2 R P, a 15 year old schoolboy, had an enlarging mass with pain in the right side of the abdomen for ten months. Abdominal discomfort, weakness, ease of fatigue, loss of 19 pounds in weight occurred. The boy was able to eat well but was quickly satisfied. The only abnormalities on physical examination were minimally enlarged axillary lymph nodes and a large mid abdominal mass. Peripheral blood examination showed no abnormality. Stools were strongly positive for occult blood. X-ray examination of the intestinal tract showed a mass in the right lower quadrant displacing small intestinal loops and deforming the cecum. Biopsy of an axillary node showed no abnormality. The patient was given a test of x-ray irradiation to the abdominal mass and when there was slight reduction in the size further irradiation was given. Two months later a re-examination of the upper

gastrointestinal tract showed involvement of the duodenum with widening of the duodenal loop and irregular deformity of the lumen presumably by a combination of intrinsic and extrinsic involvement (Fig. 3 A-2). Four weeks later, further persistent nausea and vomiting occurred. The patient became progressively worse and died nine weeks after initial hospitalization. At autopsy enlarged matted lymph nodes compressing the duodenum and common bile duct were present with invasion of the pancreas. Sections of nodes showed lymphosarcoma.

CASE 3. M. W., a 58-year-old housewife, died for thirty-five years had recurrent upper abdominal discomfort, belching and occasional vomiting. Two months before admission persistent vomiting developed. Physical examination and routine laboratory studies showed no definite abnormalities. X-ray examination showed marked distention of about 4 feet of the proximal small bowel (Fig. 3 A-3). At laparotomy an unusual constricting lesion of the lower jejunum was found and resected. Pathologic examination showed adenocarcinoma of the jejunum. Death occurred eleven days postoperatively and autopsy showed metastases to regional lymph nodes and gangrenous peritonitis.

CASE 4. B. G., a 41-year-old housewife, had her first episode of severe abdominal pain with tenderness and vomiting four months before admission to the hospital. Five days before admission nausea, retching and severe colicky and abdominal pain appeared. The pain was severe enough to require morphine. The inability to eat persisted and the abdomen became distended. Physical examination showed an acutely ill dehydrated woman. The abdomen was distended and tender and a poorly defined mass was palpable in the left mid abdomen. Examination of the intestinal tract showed an abnormal loop of proximal jejunum (Fig. 3 B-1, 2). With persistence of the colicky pain and abdominal distention laparotomy was advised. A thickened inflamed segment of jejunum 14 inches in length was found and removed. Pathologic examination of the resected specimen showed a severe non-specific ulcerative enteritis.

CASE 5. F. D., a 44-year-old housewife, was admitted to the hospital complaining of recurrent abdominal pain, distention, and slight constipation of two weeks duration. The pain sometimes radiated to the right scapula and was partially relieved by small amounts of food taken at frequent intervals. During her two weeks illness the patient had also noted a daily temperature elevation to 100°F . A somewhat similar attack of fever and abdominal pain had subsided spontaneously seven years previously. Physical examination showed gaseous distention and tenderness in the upper half of the abdomen. X-ray examination of the gastrointestinal

tract showed a long abnormal segment of proximal jejunum (Fig. 4 A-1, 2). On the eighth hospital day an exploratory laparotomy was performed. Excessive clear peritoneal fluid was present and the jejunal loops were thickened, edematous and reddened. No resection or anastomosis was done. During the following seventeen months the patient became free of abdominal distress. X-ray examination at this time showed a considerably more normal appearing small bowel (Fig. 4 A-3).

CASE 6. T. H., a 22-year-old grocery clerk, when about fifteen or sixteen years of age had had two episodes of severe bloody diarrhea thought to result from bacillary infection. He was well thereafter until two months before admission to the hospital when colicky abdominal pain, loose stools, vomiting, urticaria and weakness appeared. His weight fell from 128 to 100 pounds. X-ray examination of the gastrointestinal tract showed dilatation of the small bowel for 3 feet from the duodenum with complete obstruction at the lower jejunum (Fig. 4 B-1, 2). Surgical exploration showed the jejunum to be thick, edematous and studded with scrofula tubercles. The diseased segment was resected and in eventual recovery ensued. Pathologic diagnosis was severe chronic catarrhal enteritis without evidence of tuberculosis.

CASE 7. I. S. had been operated upon at his local hospital for a suspected rupture of the appendix and an inflammatory mass had been found involving the cecum but the appendix could not be identified. He was transferred to the University Hospital where two weeks later x-ray examination of the colon and upper gastrointestinal tract was carried out. A constricting deformity of the cecal tip with associated deformity of the terminal segment of the ileum was found. This was considered to be compatible with peripendicular abscess (Fig. 5 A-1). The lower abdominal mass diminished slightly in size with sulfadiazine and penicillin therapy. At operation some weeks later, an inflammatory mass was found to involve the cecum and terminal ileum. It was thought that a transected appendiceal stump was identified. Recovery was uneventful.

CASE 8. G. W., a 19-year-old farm girl, had had an abrupt onset of bloody diarrhea with three to eight stools a day when ten years of age. Along with the diarrhea she had spells of abdominal distention, cramp-like pain and occasionally vomiting. She was studied at the University Hospital eight months after the illness began when she was found to have a severe anemia and roentgen evidence of chronic ulcerative colitis. Throughout the succeeding year she had fluctuating anemia, fever and bloody diarrhea. With bowel movements she had cramping pains in the lower abdomen. Eight months before her second hospital admission she developed a urticaria which persisted for two or three

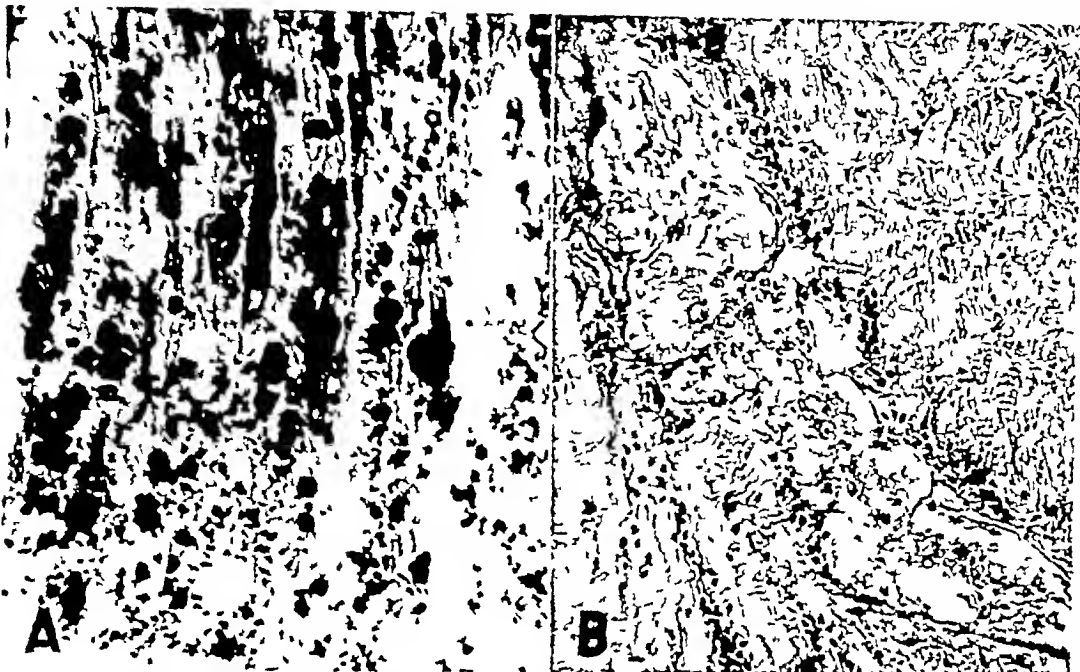


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months. During the juncture she had a mildly sore tongue as well as cracks at the corners of her mouth. Examination on the second admission showed her to be small, pale and appearing at least five years younger than her stated age. The abdomen was somewhat distended and the liver and spleen were slightly enlarged. There was a severe anemia with a red blood count reduced to 1.4 million and hemoglobin to 16 gm. The red cell size was about half normal. The stools contained mucus and gross blood. Roentgen examination of the intestinal tract again showed abnormalities typical of ulcerative colitis and in addition involvement of the terminal ileum (Fig 5, A 2).

CASE 9. G. R. a 25 year old white female, had for ten years had moderately advanced tuberculosis with recurrently positive sputum. Sixteen months before admission to the hospital a mass appeared in the right lower quadrant of the abdomen which was particularly noticeable after meals. A dull aching pain in this region with fever and occasionally nausea and vomiting developed. Physical examination showed a firm, tender, fixed mass in the right lower abdomen. The sputum continued tubercle bacilli. Roentgenographic examination (Fig 5, A 3) showed extensive deformity and narrowing of the terminal ileum and cecum and a constricted segment in the transverse colon. At operation extensive tuberculous involvement of the ileum and cecum was found. An ileosigmoidostomy was done.

CASE 10. C. H. a 35 year old male, began to have diffuse pain in the lower abdomen, belching and flatus at the age of seventeen years. An appendectomy was done in 1923 several months after the symptoms had appeared but his condition did not improve. Subsequently he had periods of nausea, generalized abdominal cramps, and pain, with swelling in the right lower quadrant of the abdomen. Watery diarrhea alternated with severe constipation. Finally persistent vomiting occurred, continuing for over a year, during which time the weight fell from 190 to 115 pounds. A severe anemia, a smooth tongue and clubbed fingers with spoon nails developed. The upper abdomen was explored in 1935, at which time numerous adhesions between the abdominal viscera were broken up. Again there was no improvement in symptoms, and several months later the patient was referred to the University Hospital.

A severe macrocytic anemia was present. Examination of the gastro intestinal tract (Fig 5, B 1, 2) showed widespread alteration of the small bowel, with delay in transit, increased caliber, and loss of normal mucosal pattern. The nutritional deficiencies and anemia were corrected with specific therapy, although chronic diarrhea remained. In July 1936, the patient became worse and at operation a distended segment of the ileum above the ileocecal junction, with two localized constrictions, was

found. The mesentery was thickened and edematous. Two feet of diseased ileum were resected. Pathologic examination of the specimen (Fig 5, B 3) showed localized mucosal ulceration with scarring and inflammation throughout the thickened gut wall.

During the following eight years the patient continued to have diarrhea with abdominal distention, easy fatigue, and a macrocytic anemia requiring liver therapy. There was no particular progression in his intestinal symptoms but his last admissions to the hospital were occasioned by the development of an acute chlororetinitis and optic neuritis.

CASE 11. M. K. a 47 year old woman, had for six years had regurgitation after eating, with a feeling of food lodging under the lower part of the sternum. She improved after esophageal dilatation. Two years before her admission she suffered from gaseous distention, belching, early morning vomiting and extreme constipation, which finally required the constant use of castor oil and enemas. On a few occasions stools were loose but did not contain blood. The weight gradually fell from the average 118 to 90 pounds. The appetite and desire for food remained good. Examination showed a very thin woman without evidence of vitamin deficiency or anemia. The intestinal loops were visibly distended. No neurologic abnormalities were detected on detailed search except for a questionable extensor plantar sign. Other than the abnormal roentgen findings in the gastro intestinal tract (Fig 6 A 1, 2, 3, B 1, 2, 3) the only abnormality was a persistent elevation of the basal metabolic rate.

CASE 12. E. R. a 27 year old farmer's wife, became ill for the first time sixteen months before her admission to the hospital with a low grade fever and pain, swelling and reddening about the ankles. She remained in bed for seven weeks. During convalescence diarrhea appeared for a time and then recurrent distention of the abdomen, occasional vomiting and unusual flatus. The symptoms continued and the average weight of 115 pounds fell slowly to 87 pounds. Examination showed emaciation, distention of the abdomen and edema of the ankles. There was no evidence of vitamin B deficiency. There was no significant anemia and no evidence of neurologic disease except for roentgenographic demonstration of intestinal dysfunction (Fig 7, A 1, 2, 3, B 1, 2). The patient was treated with a nutritious diet, vitamin supplements, yeast, calcium, intramuscular and intravenous liver extracts, and parasympatheticomimetic drugs. There was no significant response to therapy and eight months after her first admission tetany developed and death occurred. Pathologic examination showed extreme atrophy of all the organs, malnutrition, muscular atrophy, and diffuse fibrosis of the intestinal walls. Marchi preparations of the spinal cord and sciatic nerve showed advanced myelin degeneration.

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SUMARIO

Estudio Radiológico del Intestino Delgado I Enfermedades Neoplásicas e Inflamatorias

Entre los muchos enfermos que presentan síntomas imputables al intestino delgado, un grupo relativamente pequeño revela signos roentgenológicos bien definidos y típicos de afección inflamatoria y neoplásica. Al postular la existencia de tales procesos, el radiólogo se atiene en general a la presencia de deformidades de la luz intestinal, desplazamiento de los segmentos intestinales y signos de obstrucción de la luz. Sin embargo, no se define con mucha claridad la línea divisoria que separa las enfermedades neoplásicas e inflamatorias de los estados derivados de trastornos neurológicos.

Aun con un sencillo procedimiento corriente de diagnóstico el radiólogo puede averiguar mucho acerca del estado del intestino delgado. El plan de examen de los AA consiste en una breve observación roentgenoscópica limitada al tiempo de la comida de bario y a los pocos momentos exigidos para seguir el paso del bario bien adentro en el yeyuno, seguido esto de la toma de películas inmediatamente y a plazos de 1, 2 1/2, y 5 horas. Mas de 100 pacientes fueron estudiados en esta forma, y se comunican 12 casos con grabados que muestran las alteraciones radiológicas en varias lesiones orgánicas y en los trastornos funcionales.



X-Ray Signs of Altered Alimentary Function Following Autonomic Blockade with Tetraethylammonium¹

JOHN F HOLT, M D, RICHARD H LYONS, M D, ROSALIE B NELIGH, M D, GORDON K MOE, M D, and FRED J HODGES, M D

THE USE OF DRUGS does not play as important a role in the practice of diagnostic roentgenology as in many of the other medical specialties and, accordingly, the roentgenologist's activities in the field of pharmacology are understandably limited. His interests quite naturally are centered chiefly upon those drugs which he can put to practical use in his daily work—agents such as amyl nitrite for the temporary relief of cardiospasm, prostigmin to rid the intestinal tract of gas, and morphine to produce sphincteric contraction at the ampulla of Vater. In general, these drugs have been adopted for use in roentgenology only after their physiologic action has been adequately studied by various laboratory methods. On the other hand, it has become increasingly apparent that the roentgenologist can be of considerable assistance to the physiologist in the evaluation of unknown or questionable properties of certain drugs, particularly in regard to their actions on the digestive tract. It was largely for this reason that roentgenologic assistance was sought in a study of some interesting properties of tetraethylammonium. Superficially, at least, this agent appeared to have potentialities of being useful both practically and from the standpoint of explaining certain poorly understood aspects of gastro intestinal physiology.

PHARMACOLOGIC BACKGROUND

Tetraethylammonium is a quaternary ammonium compound structurally similar to acetylcholine. In 1945, Acheson and

Moe (1), working on heart-lung preparations of dogs, noted some interesting effects of the tetraethylammonium ion which had not been previously reported. Subsequent animal experiments (2, 3), in which reactions of the blood pressure, heart rate, and nictitating membrane were used as test responses, indicated that intravenous or intramuscular injections of the drug produced a rather specific blockade of the transmission of nerve impulses through sympathetic and parasympathetic ganglia.

CLINICAL ASPECTS

Clinical experimentation (4, 5) showed that parenteral administration of tetraethylammonium produced widespread autonomic nervous system effects consisting of postural hypotension, increase in skin temperature and blood flow in the extremities, elevation of the cardiac rate, cessation of sweating, dry mouth, fixation of the pupils in mid-dilatation, loss of ocular accommodation, and inability to void. Certain hypertensive subjects showed a significant drop in both systolic and diastolic blood pressure, and in the case of one such patient who also had a duodenal ulcer, the ulcer pain stopped completely during the period of activity of the drug. Additional investigation of this patient showed that gastric secretion was markedly decreased by the drug, but that the pain disappeared long before the stomach emptied itself of secretions already present. This finding would seem to support the concept that peptic ulcer pain is caused primarily by smooth muscle spasm,

¹ From the Departments of Roentgenology, Internal Medicine and Pharmacology, University of Michigan, Ann Arbor, Mich. Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.

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Tetraethylammonium was supplied as "Etamon" by the Department of Clinical Investigation, Parke, Davis and Co., Detroit, Mich.



Fig 1. A (2-27-46) Normal control. Stomach filled with 6 oz. of barium sulfate.
 B (3-1-46) Similar quantity of barium in same patient's stomach a few minutes following intravenous injection of 2 cc. of a 10 per cent solution of tetraethylammonium. Note generalized loss of muscular tone, absence of peristaltic waves, and lack of emptying at the gastric outlet. Appearance similar to atonic stomach following vagotomy (Fig 2-B).

and not by the mere presence of acid in the stomach or duodenal bulb.

Administration of tetraethylammonium also has been found to relieve the pain and to increase the skin temperature in various peripheral vascular diseases associated with vasoconstriction. The ability of the drug to relieve vasospasm has also made it a useful diagnostic tool in assaying sympathetic tone in candidates for lumbar sympathectomy. It appears to be of limited value in the symptomatic treatment of hypertension.

ROENTGENOLOGIC OBSERVATIONS

As roentgen methods offer the most rational means of detecting altered physiologic function in the alimentary canal of man, this approach was employed in a study of the effects of tetraethylammonium on the esophagus, stomach, small intestine, and colon.

Esophagus and Stomach It was hoped that tetraethylammonium, through its blocking action on the autonomic ganglia, might prove to be more effective in the relaxation of cardiospasm than amyl nitrite, which acts directly on smooth muscle. Four patients with cardiospasm were tested. None responded to tetraethylammonium, two showed prompt relaxation following amyl nitrite inhalation. An explanation for this apparent paradox may be found in the works of Etzel (6), Knight (7), and others, who maintain that cardiospasm is due to degeneration of the nerve plexuses in the walls of the esophagus. If such is the case, a drug which acts on nerve cells rather than on the muscle itself would have little or no effect.

Tetraethylammonium produced no visible alteration in the appearance of the normal esophagus.

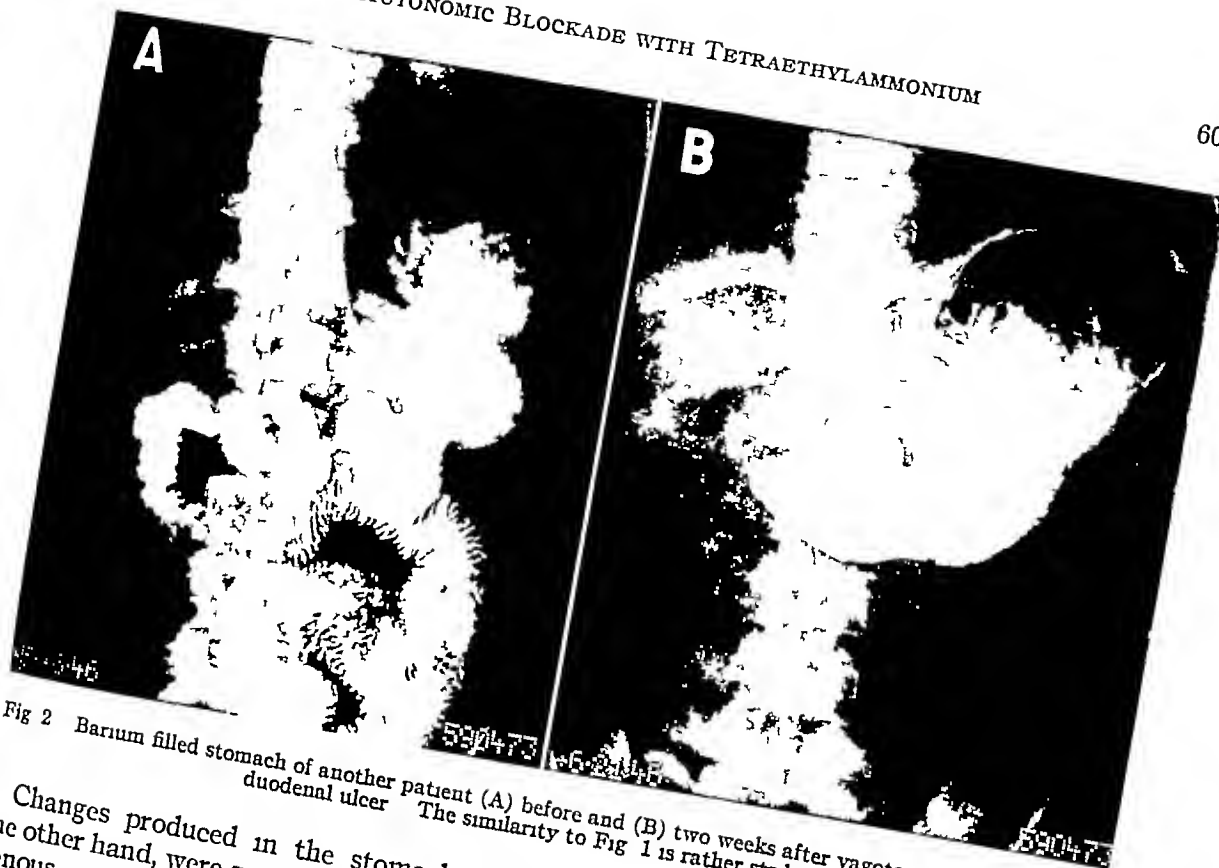


Fig 2 Barium filled stomach of another patient (A) before and (B) two weeks after vagotomy for treatment of duodenal ulcer. The similarity to Fig 1 is rather striking

Changes produced in the stomach, on the other hand, were quite definite. Intravenous injection of tetraethylammonium resulted in prompt diminution of gastric muscular tone and generalized dilatation of the stomach. All signs of peristaltic activity except a few marginal fibrillations stopped abruptly and remained quiet during the period of activity of the drug (Fig 1). There was no appreciable escape of barium through the pylorus. With few exceptions, intramuscular injections of tetraethylammonium produced the same results except that the effects of the drug appeared more slowly and lasted over a longer period of time. In either case, the over-all appearance of the stomach was strikingly similar to that seen following vagotomy (Fig 2).

Small Intestine Considerable attention was given to a study of tetraethylammonium effects on the small bowel, a structure whose complex autonomic neuromuscular mechanism is still a subject of dispute. Normal small intestinal function is largely dependent upon maintenance of a delicate balance between the sympathetic

and parasympathetic components of the autonomic nervous system. Propulsive movements are readily influenced by the extrinsic nerves, *viz*, the vagus (parasympathetic), which furnishes motor stimuli except at the sphincters, and the splanchnics (sympathetic), which are inhibitory except in sphincteric control. Similar peristaltic contractions also may be accomplished through entirely local myenteric reflexes occurring within two highly important intramural plexuses. These are the myenteric plexus of Auerbach, located between the muscle coats, and the submucosal plexus of Meissner. In view of the ganglionic action of tetraethylammonium, it should be pointed out that the parasympathetic preganglionic fibers terminate in the intramural plexuses, thus the parasympathetic ganglia and postganglionic neurons are located entirely within the intestinal wall. On the other hand, sympathetic preganglionic fibers terminate in the celiac and mesenteric ganglia which in turn send long postganglionic fibers directly to the muscle layers of the intestinal wall.

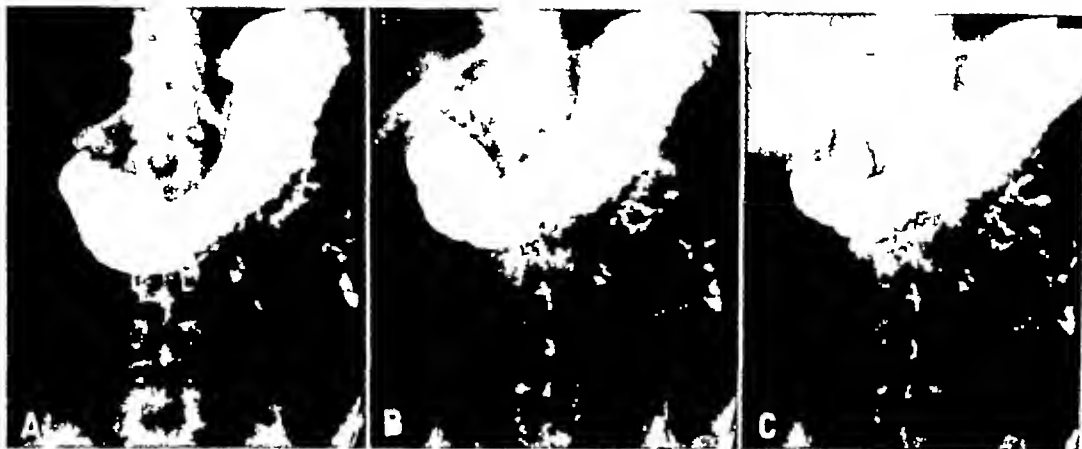


Fig 3 A Appearance of stomach and proximal small bowel of a 40 year-old woman shortly after intra-muscular injection of 1.5 gm of tetractylmmonium. Profound disturbance in motility following use of this drug is exemplified by exposures B and C made one and two hours respectively after ingestion of barium. The mucosal pattern in the duodenum and jejunum shows no appreciable change during these long intervals

Forssell (8) states that the intestinal mucosa moves independently of the outer muscular layers which produce peristalsis, an observation which Golden's (9) roentgenologic studies appear to confirm. Both men believe that the motor stimuli responsible for changes in the mucosal folds are supplied by sympathetic nerve fibers *via* the submucosal plexus.

The well-known rhythmical contractions of the small intestine (so called pendulum movements) supposedly are not under control of the nervous system, but are entirely dependent upon the inherent contractile power of intestinal smooth muscle.

It will be remembered that, despite brilliant pioneer work by Forssell (10), Cole (11), and others, little attention was centered on the small intestine by roentgenologists until 1933 when Mackie (12) described abnormal changes in the form and action of the structure in a patient with sprue. Soon afterward, Snell and Camp (13) noted delayed motility and distortion of the mucosal pattern of the jejunum in chronic idiopathic steatorrhea, it was suggested that the abnormalities seen probably were not diagnostic of sprue but would be found in other conditions as well. Subsequent reports of similar functional small bowel disorders in a wide variety of primary and secondary nutritional

disorders, various allergic conditions, and organic diseases of the digestive tract proved the accuracy and wisdom of Snell and Camp's prophecy. The non-specific roentgen manifestations of altered intestinal motility and tone, abnormal segmentation of the barium column, and coarsening or obliteration of the mucosal folds came to be commonly known as the "deficiency pattern." This useful but somewhat inadequate term has been largely supplanted by the more descriptive term "disordered motor function."

Golden (9) has postulated that the apparently unrelated conditions which manifest "disordered motor function" have a common mechanism through which they are produced. He maintains that the fundamental fault lies in derangement of the intricate and poorly understood intramural nerve plexuses. Golden's theory is based on sound physiologic experimentation by numerous investigators, convincing neuropathologic findings, and extensive roentgenologic observations. The theory has not been universally accepted, but that it represents a plausible explanation of an intriguing problem cannot be denied.

Additional support to Golden's "neurogenic theory" has been contributed recently by Hodges, Rundles and Hanelin (14), who have observed small bowel dys-



Fig 4 Small bowel enema outlining virtually entire small intestine of a 56 year old man, weight 179 pounds
 A Exposure made immediately following intramuscular injection of 1.6 gm of tetraethylammonium B Same patient thirty minutes later The mucosal pattern of the intestine has not changed perceptibly

function occurring frequently in patients with various types of peripheral neuropathy. They suggest that in such patients, transient or permanent autonomic nervous system damage is responsible.

With this background in mind, it was felt that the roentgenologic appearance of "disordered motor function" might very well be produced artificially by paralyzing both parasympathetic and sympathetic ganglia through the unique action of tetraethylammonium.

A total of twelve small bowel examinations was made on eight different subjects, all of whom were well nourished, and none of whom had symptoms or signs referable to the gastro-intestinal tract. Preliminary control examinations were done where they were deemed essential. As a rule, fluoroscopic and roentgenographic survey of the barium-filled intestine prior to injection of tetraethylammonium satisfied this requirement.

An outstanding finding in every patient who received either intravenous or intra-

muscular injections of the drug was the profound degree to which propulsive movements of the intestine were inhibited. Even in the duodenum and proximal jejunum, where peristalsis is most vigorous, motility appeared to stop completely (Fig 3). Fluoroscopically, it appeared as if one were observing the intestinal tract of a cadaver outlined by opaque medium.

Of further interest was the fact that in many instances careful search both at the screen and on multiple films failed to show the usual undulating, pendulum movements which are so common in the lower portion of the small bowel and which supposedly are entirely myogenic in origin. This rather dramatic cessation of intestinal movements lasted for only a few minutes following intravenous injection of tetraethylammonium, whereas an intramuscular dose of 20 mg/kg produced similar changes which persisted for as long as three hours.

Perhaps the most striking change of all in this series of observations was the man-

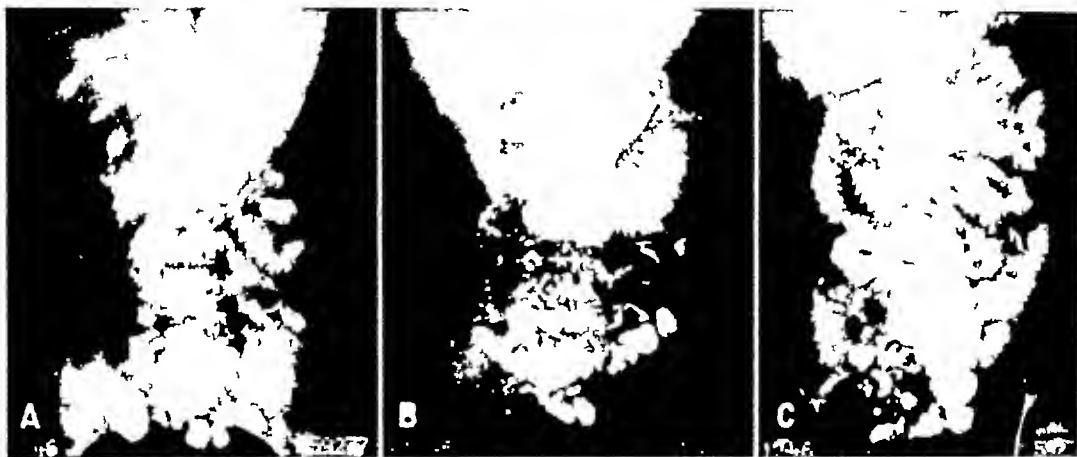


Fig 5 A Normal feathery pattern of jejunum in a 16 year old girl Head of barium column has entered proximal ileum

B Several minutes after intramuscular injection of 12 gm of tetraethylammonium fluoroscopy showed the small bowel to be frozen in this somewhat abnormal pattern (the change may be entirely coincidental)

C Ten minutes after subcutaneous injection of 25 mg of mecholyl peristalsis was seen to be very active and distribution of barium appeared more normal

ner in which the mucosal markings of the small intestine appeared to be fixed in one position by tetraethylammonium over a period of minutes or hours. This feature was not a constant finding in every case, but it occurred too often to be considered merely coincidental. The phenomenon was shown to best advantage following a small bowel enema. Employing the technique described by Schatzki (15), the entire small bowel was filled with barium, and fluoroscopy showed intestinal movements to be quite active. The usual intramuscular dose of tetraethylammonium was injected, and within three or four minutes all intestinal movements had stopped. Interval films showed no perceptible change in the pattern of the mucous membrane folds over a period of thirty minutes (Fig 4).

It must be admitted that all features of a well defined "deficiency pattern" of the small intestine were not produced in most of the patients examined. In addition to profound disturbances in motility, however, some degree of coarsening of the mucosal markings and slight generalized dilatation of the entire small intestine usually were evident. Thus, the appearance of the bowel could not be considered entirely normal.

In one patient, marked variation in

the caliber of the intestinal lumen appeared immediately after injection of tetraethylammonium, and this was associated with abnormal segmentation of the barium column and the usual absence of propulsive movements. Subcutaneous injection of acetyl-beta-methyl choline (mecholyl), through its direct action on smooth muscle, immediately precipitated peristalsis and, at the same time, gave the mucosal pattern a more normal appearance (Fig 5).

Atropine alone, through its paralyzing action on the parasympathetic nervous system, and adrenalin, which stimulates the sympathetics, were found to produce some inhibition of intestinal motility, but the degree of change was not so pronounced as it was with tetraethylammonium. Furthermore, regular movements of the mucosa persisted despite large doses of either atropine or adrenalin.

Colon. Changes in motility of the colon are difficult to detect because progress of the barium meal in this region is so slow. Tetraethylammonium produced no appreciable change in the haustral pattern of the normal colon, although it was found that during the period of activity of the drug, the large bowel could be markedly distended without producing a desire to defecate.

SIGNIFICANCE OF FINDINGS

The admittedly limited observations herein reported bring up a number of questions concerning gastro-intestinal physiology which, in the present state of our knowledge, must remain unanswered or, at best, be subject to mere speculation. These questions will be dealt with in a subsequent publication (16) following more extensive laboratory experimentation and a more careful correlation of the data thus far obtained with existing anatomical and physiological facts.

SUMMARY

Tetraethylammonium is a simple organic compound which possesses a recently recognized property that is unique among known pharmaceutical agents. Parenterally administered, the drug appears to block the transmission of impulses through the autonomic ganglia—both sympathetic and parasympathetic.

Preliminary roentgenologic observations indicate that the drug produces diminution of gastro-intestinal tone and causes virtually complete cessation of motility in the small bowel. In many instances, movements of the small intestinal mucosal folds are completely stopped for relatively long periods of time. This is in contradistinction to the action of atropine and adrenalin, both of which produce some decrease in motility but neither of which has any appreciable effect on mucosal movements.

Artificial paralysis of autonomic ganglia does not consistently produce all of the classical roentgenologic features of "disordered motor function" of the small intestine as seen in various nutritional disorders, gastro intestinal allergy, diabetic neuropathy and other conditions.

Although the therapeutic value of tetraethylammonium at present is distinctly limited, further study of its properties may find it a place in medical management. In the meantime, the drug should prove to be a useful agent in further investigation of both the normal and disordered autonomic nervous system.

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University Hospital
Ann Arbor, Mich

DISCUSSION

Walter L. Palmer, M D (Chicago). This has been a fascinating paper. It raises, of course, many questions and many problems for discussion. I wish merely to discuss the mechanism of ulcer pain.

The relief of ulcer pain by the use of tetraethylammonium was interpreted as evidence that the pain is caused by smooth muscle spasm. I would suggest that it does not constitute such proof at all. The pain of duodenal ulcer is due to acid acting on

the surface of the ulcer. The drug immediately halts peristaltic activity and stops the emptying of the stomach, as the authors have shown quite conclusively. Anything which does that will immediately relieve the pain of a duodenal ulcer, because the surface of the lesion is then bathed with alkaline duodenal content.

Of course, when an ulcer is sensitive pain can be

induced by muscle spasm, but the sensitivity of the ulcer itself is produced by the action of the acid. Pain is ordinarily due to the action of the acid gastric juice. I think we can interpret the relief of pain from tetraethyl ammonium as due to the prompt cessation of gastric emptying, so that the ulcer is bathed with the alkaline duodenal contents instead of the acid gastric juice.

SUMARIO

Signos Radiológicos de Disfunción Alimenticia Consecutivamente a Bloqueo del Autónomo con Tetraetilamonio

El tetraetilamonio es un compuesto orgánico simple que posee una propiedad, reconocida recientemente, que es única para los elementos farmacéuticos, y que consiste en que, administrada parentéricamente, la droga parece bloquear la transmisión de impulsos por los ganglios del sistema autónomo, tanto del simpático como del parasimpático.

Las observaciones roentgenológicas preliminares indican que la droga atenúa la tonicidad gastrointestinal y hace cesar, virtualmente por completo, la movilidad del intestino delgado. En muchos casos, se paran completamente los movimientos de los pliegues de la mucosa de dicho intestino durante períodos relativamente largos de tiempo. Esto es en contraposición al efecto de la atropina y la adrenalina,

pues aunque ambas provocan alguna disminución de la movilidad, ni una ni otra ejercen efecto apreciable sobre los movimientos de la mucosa.

La parálisis artificial de los ganglios del autónomo no produce constantemente todas las clásicas características radiológicas de la "disfunción motriz" del intestino delgado, tal como se observa en varios trastornos nutritivos, la alergia gastrointestinal, la neuropatía diabética y otros estados.

Si bien el valor terapéutico del tetraetilamonio es hoy día bien limitado, el estudio ulterior de sus propiedades puede encontrarle un puesto en la asistencia médica. Entre tanto, la droga debe resultar útil para nuevos estudios del sistema nervioso autónomo tanto normal como trastornado.



Acute Obstruction of the Small Bowel

Value of Roentgen Examination in Early Diagnosis¹

JACK SPENCER, M D, and LANGDON T THAXTER, M D

Portland, Maine

THE MATERIAL for this paper has been collected during the past fifteen years from the records of the Maine General Hospital, where it has been a routine procedure during this period to take a "scout film" in all undiagnosed acute abdominal cases, particularly cases in which intestinal obstruction is suspected. Three hundred and fifty cases of either small or large bowel obstruction have been studied. Of these, 100 cases have had both roentgen-ray studies and surgical confirmation of the diagnosis of small bowel obstruction.

The purpose of this paper is to correlate the roentgen with the surgical findings in this latter group of cases. It is further our purpose to show, as has frequently been reported by others, that with adequate roentgen study, not only is the diagnosis highly accurate, but the location of the lesion may be approximated in a large percentage of cases and in some the nature of the obstruction may be anticipated. Cases of external hernia and of carcinomatosis and peritonitis, where the obstruction was of secondary importance, have been excluded. This corresponds to reports from the Massachusetts General Hospital by Scudder, Richardson, McIver, McKittrick and Sarris.

Since Case, in 1920, reported on "a new aid in the early recognition of postoperative ileus," a mass of literature has appeared on this subject. This has been adequately reviewed in the recent books of Wangenstein and Golden and no attempt will be made to reduplicate their extensive studies

ROENTGEN STUDY

For the past fifteen years, it has been our routine practice to obtain a "scout

film" in all acute abdominal cases. This is studied immediately. If further information is desired, an upright film may be taken including the diaphragm, to determine the presence of a pneumoperitoneum or fluid levels. A decubitus film with the right or left side up, or a lateral view in the supine position if the patient is acutely ill, will give the same information and will also help to identify further the point of obstruction. In the study of all films the following points are kept in mind:

1. Abnormal gas shadows, due to
 - (a) Intestinal tract (what part?)
 - (b) Pneumoperitoneum
 - (c) Air in biliary tract
2. Possible causes of mechanical or reflex ileus
 - (a) Gallstones
 - (b) Renal stones
 - (c) Fecaliths
 - (d) Foreign bodies
3. Abnormal soft-tissue shadows
4. Bone abnormalities

For the purpose of this analysis, the presence of abnormal intestinal gas will be discussed. Air in the small bowel, except in the very young, is abnormal but does not necessarily indicate obstruction.

After an enema, fluid and gas may pass through the ileocecal valve into the small bowel, but in such cases the gas is minimum in amount and is limited to the terminal ileum, which shows no dilatation. Occasionally in the presence of a large bowel obstruction segments of small bowel may show dilatation. In one of our cases this was explained on the basis of obstruction not only of the large bowel but also of the terminal ileum.

The occurrence of gas in the small bowel after instrumentation for retrograde pyelography is a familiar observation and the

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¹ Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec. 1-6, 1946.



Fig 1 Case of renal colic with gas in the large and small bowel. A segment of small bowel in the region of the left sacroiliac joint is outlined with gas, and mucosal folds (Kerkring's folds) can be identified. There is no evidence of mechanical obstruction in this case.

same holds true for any acute abdominal pain. At times it may be difficult to decide whether this gas is of primary importance, but usually the history, plus the fact that the bowel is not dilated, will help to determine the significance of these changes (Fig 1). The important point, therefore, is not only whether or not gas is present, but whether there is dilatation of the small bowel.

An attempt should be made to determine the location of the gas and thereby estimate the location of the obstruction. In general, it may be stated that the jejunum is mostly in the left upper abdomen, extending to the left lower quadrant, while the ileum is to the right, extending into the right lower quadrant and pelvis. When the bowel is markedly distended however, the positions may be altered so that this observation, though it may be quite helpful, is not entirely dependable.

The anatomical characteristics (Table I) give the most important information. The lumen of the jejunum is the widest part of

the small intestine. The circular or transverse mucosal folds (valvulae conniventes or Kerkring's folds) are higher, closer, and thicker than those of the ileum and cannot be obliterated. The ileum has a narrower lumen, the mucosal folds are fewer in number, are slender, shallow, and can be obliterated in the distended segments. With a small amount of gas in the jejunum

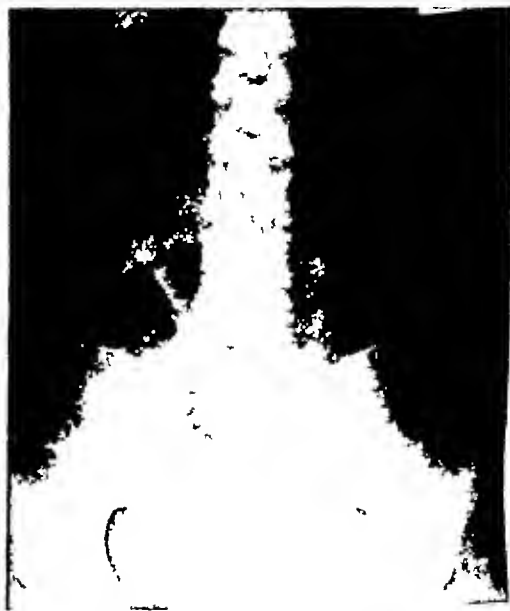


Fig 2 "Hairpin" loop of dilated small bowel due to adhesions causing early obstruction of ileum.

a typical "feathery" appearance is evident, which changes to a "herring-bone" or "coil-spring" pattern as dilatation increases. The wall, therefore, appears straighter and thinner (Fig 3).

In lower jejunal obstruction the mucosal folds become straighter, giving a "squaring" of the segments. For this reason it is sometimes difficult to distinguish this portion of the small bowel from the colon. In such cases a barium enema may be necessary for differentiation. In selected cases further study by means of the Miller-Abbott tube and barium injection may be helpful in localization.

As the more distal segments of the ileum are involved, the mucosal folds become fewer, wider apart, and more easily ob-

TABLE I ANATOMICAL AND ROENTGEN RAY CHARACTERISTICS OF INTESTINAL TRACT

	Jejunum	Ileum	Colon
Location	Left upper quadrant	Right lower quadrant	Laterally, except for transverse colon, which can be seen in continuity with lateral portions
Thickness of walls	Thick	Thin	Thicker
Lumen	Widest part of small intestine	Not so wide as jejunum	Widest portion of intestine
Mucosal folds (circular folds)	Kerkring folds Higher Closer Thicker	Circular folds Shallower Fewer Thinner	Coarse haustral markings
Appearance with distention	'Feathery' appearance with a small amount of gas 'Herring bone' or 'coilspring' appearance as distention increases Straight thin walls Fluid levels	Characterless appearance, with folds becoming obliterated Fluid levels	Haustral markings with scalloped effect Long single fluid level

In mid bowel (low jejunum and upper ileum) the 'coilspring' appearance is lost and folds become straight, giving a 'squaring' effect 'Hairpin' loop early or partial obstruction Ladder formation late obstruction

literated, giving a "characterless" appearance to the markedly dilated loops

The colon is distinguished by its haustral markings and the fact that it lies laterally, except for the transverse colon, which is in continuity with the lateral areas. Its walls are thicker and dip downward, the haustral markings giving a scalloped appearance

ANALYSIS OF DATA

The roentgen findings indicating small bowel obstruction were conclusive in 94 cases out of 100 (Table II). Of the inconclusive cases, one was observed for three days and on the final film small bowel obstruction was diagnosed. Another case was observed for three days with a Miller-Abbott tube inserted. The findings were suggestive but not conclusive of obstruction due to decompression by suction. In both of these cases an obstruction was found at operation. In a third case no gas was seen and no fluid levels were present on any of the films, but at operation there was a definite obstruction 30 cm from the ileocecal valve. The bowel above the obstruction was markedly distended with fluid but contained practically no gas.

In 50 cases the location of the obstruction was stated in the operative notes. The films on these cases were studied without reference to the operative record and

the location of the obstruction given at one of three levels, namely, jejunum, mid small bowel (low jejunum and upper ileum), and terminal ileum. In every instance the approximate level as determined from the roentgenogram corresponded to the operative finding. The obstruction was in the terminal ileum in 33 cases, in the mid small bowel in 9 cases, and in the jejunum in 6 cases. In 8 cases a barium enema was necessary for localization of the gas.

There were 2 cases with negative findings when first examined, but during an attack of intestinal colic a dilated loop of small bowel was seen. This examination was suggested by Dr Isaac M. Webber.

The cause of the obstruction could be determined in only 5 cases. In one case a gallstone was seen in the jejunum, which was dilated above the site of obstruction. Also gas was visible in the gallbladder, indicating a fistula between the gallbladder and intestinal tract (Fig. 8). In another, air was seen in the gallbladder and the stone was also demonstrated (Fig. 7).

There were 4 cases of intussusception. One was diagnosed as due to a carcinoma of the cecum (Fig. 9). In another, the intussusception was suspected as the cause of the obstruction. Two others were due to fibromata of the small bowel, but only the resulting obstruction was diagnosed.

In another case, the cause and location of



Fig 3 Early high jejunal obstruction Note 'feathery pattern' of dilated jejunum

Fig 4 Low jejunal obstruction (compare with Fig 3) Note that dilatation is greater, the feathery pattern is replaced by a herring bone pattern and the folds are apparent in the mid jejunal loop just above the left iliac crest



Fig 5 Obstruction at terminal ileum Note herring bone pattern and ladder formation of jejunum in the left upper quadrant and left lower quadrant

Fig 6 Same case as Fig 5 after barium enema

Operation showed an adhesive band causing obstruction between the terminal ileum and ascending colon



Fig 7 Obstruction due to gallstone with air in the gallbladder also demonstrated

Fig 8 Gallstone causing obstruction Air in the biliary tract is demonstrated The gallstone is not identified but was found at operation

the obstruction were demonstrated by barium enema studies (Figs 10 and 11). There were adhesions between the sigmoid and the cecum, causing a partial intermittent obstruction of both, with rotation and volvulus of the cecum, the ileum being lateral to the ascending colon and also obstructed. This illustrates the fact that where there is both small and large bowel dilatation a double obstruction should be suspected, although with a single large bowel obstruction there may be gas in the small as well as the large bowel.

The causes of obstruction as determined at operation are given in Table III. In 78 per cent of the cases the obstruction was due to adhesions, and of this group of patients, 55 had had previous laparotomies. There were 3 cases due to Meckel's diverticulum which were not diagnosed as such.

A study of the mortality in this series of cases revealed 23 deaths. Of these, 7 were due to conditions other than the obstruction, reducing the actual mortality from obstruction and infection to 16 cases. Forty cases were seen before 1940, with



Fig 9 Intussusception due to tumor in the cecum. The mass is identified and gas is seen in the terminal ileum.

13 deaths (32 per cent) and 60 cases after 1940, with 10 deaths (16 per cent).



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TABLE II DATA ON 100 CASES OF MECHANICAL OBSTRUCTION OF THE SMALL BOWEL (CONCLUDED)

Hosp No	Age	Pre-vious Opera-tion	Roentgenological Conclusions	Operative Findings as to Cause of Obstruction	Survival
29430	69	No	Small bowel obstruction	Adhesions, bands	Yes
3820	70	Yes	Small bowel obstruction	Adhesions, bands	Yes
47599	50	Yes	Intestinal obstruction	Adhesive band from base of bladder to mesentery of ileum	Yes
46893	59	?	Partial obstruction	Adhesive band of omentum in region of cecum	No
51517	50	Yes	Small bowel obstruction	Adhesive bands	Yes
50037	32	Yes	Small bowel gas with slight dilatation	One adhesive band attaching loop of upper ileum to sigmoid	Yes
54267	75	Yes	Small bowel obstruction	Adhesive band from diverticulum of sigmoid to posterior wall obstructing terminal ileum	Yes
54266	43	No	Gas filled loops of small bowel with no dilatation Observed 3 days with Miller-Abbott tube, small bowel gas still demonstrated	Moderately distended small bowel due to adhesive band	Yes
47724	76	?	Probable intestinal obstruction, in ileum	Fibrous band from omentum obstructing terminal ileum	Yes
14585	78	No	Intestinal obstruction	Adhesion of ileum to gallbladder	Yes
45634	23	Yes	Partial obstruction	Pelvic adhesions with volvulus	Yes
29896	41	Yes	Dilated loops of small bowel indicating mechanical obstruction	Adhesions with volvulus	Yes
28906	22	Yes	High small bowel obstruction	Adhesions with volvulus	No
9930	41	Yes	Partial small bowel obstruction	Adhesions with volvulus	Yes
53381	42	No	Partial obstruction	Volvulus	No
4300	42	No	Partial obstruction, terminal ileum	Adhesions with volvulus	Yes
30894	70	No	Partial obstruction	Adhesions with volvulus	Yes
19070	46	Yes	Small bowel obstruction	Adhesions with volvulus	Yes
37455	58	No	Small bowel obstruction	Femoral hernia with obstruction	Yes
48305	60	Yes	High intestinal obstruction	Incisional hernia with jejunum knuckled by adhesive band	Yes
14215	81	Yes	Hernia demonstrated with dilated segment of small bowel	Strangulated femoral hernia	No
54931	76	No	Probable partial intestinal obstruction	Direct inguinal strangulated hernia (Richter type)	Yes
56704	70	Yes	Partial intestinal obstruction	Strangulated femoral hernia	Yes
16839	71	Yes	Intestinal obstruction	Large hernia	No
16603	62	Yes	Probable small bowel obstruction	Hernia through McBurney incision	Yes
42083	51	No	Ladder-like arrangement of dilated loops indicating intestinal obstruction	Femoral hernia	No
44310	31	?	Obstructing lesion in terminal ileum	Meckel's diverticulum	Yes
23082	50	Yes	Dilated loops of small bowel	Meckel's diverticulum	Yes
2645	6	No	Partial small bowel obstruction	Meckel's diverticulum with intussusception	Yes
46809	64	Yes	Partial obstruction	Fibroma, small bowel with intussusception	Yes
6498	59	Yes	Obstructing lesion near ileocecal valve	Fibromyoma	Yes
20106	56	No	Intussusception due to polypoid tumor in region of cecum	Carcinoma 10 cm above ileocecal valve, 30 cm ileum showing intussusception	Yes
38430	70	No	Small bowel obstruction caused by gallstone	Gallstone causing obstruction	No
865	66	No	Obstructive lesion in ileum	Gallstone causing obstruction 3 feet beyond ileum	No
49201	74	No	Partial intestinal obstruction	Obstruction due to gallstone	Yes
3612	55	No	Small bowel obstruction	Terminal ileitis	No
24327	57	No	Small bowel obstruction	Terminal ileitis	No
43307	23	Yes	Small bowel obstruction	Tuberculosis, terminal ileum	Yes
51422	58	Yes	Partial small bowel obstruction	Metastatic node	Yes
49299	63	No	Small bowel obstruction	Mass of adhesions	Yes
48585	70	Yes	Dilated small and large bowel	Carcinoma of colon with large and small bowel obstruction	No
24327	57	No	Small bowel obstruction	Pelvic mass	No
50341	65	Yes	Small bowel obstruction	Pelvic adhesions	Yes
34406	45	Yes	Partial obstruction	Fibrous lesion, terminal ileum	No
39193	62	Yes	First film inconclusive, 4 hours later definite obstruction	Adhesions in area of terminal ileum	Yes
				Toothpick perforated ileum 7 months previously	Yes

TABLE II DATA ON 100 CASES OF MECHANICAL OBSTRUCTION OF THE SMALL BOWEL

Hosp No	Age	Pre-vious Oper-ation	Roentgenologic Conclusions	Operative Findings as to Cause of Obstruction	Survival
38485	0	Yes	Partial obstruction	Adhesions	Yes
37591	46	Yes	Ladder formation	Adhesions	Yes
39410	30	Yes	Partial obstruction	Adhesions	Yes
32332	60	Yes	Suggestive of partial obstruction (Review of films definite obstruction)	Adhesions	No
32127	45	Yes	Ladder formation indicating small bowel obstruction	Adhesions	Yes
34576	84	Yes	Small bowel obstruction	Adhesions	Yes
51700	69	Yes	Small bowel obstruction	Adhesions	Yes
1925	64	Yes	Obstruction near ileocecal valve	Adhesions	Yes
1610	70	Yes	Partial obstruction with increase in dilatation over 24 hour period	Adhesions	Yes
5115	27	Yes	Partial small bowel obstruction	Adhesions	Yes
42053	28	Yes	Probable obstruction	Adhesions	Yes
41755	7	Yes	High small bowel obstruction	Adhesions	Yes
45266	20	Yes	Partial obstruction	Adhesions	Yes
44857	18	No	Partial obstruction	Adhesions	No
45175	36	Yes	Intestinal obstruction	Adhesions	No
36799	32	Yes	Small bowel gas but not sufficient to make diagnosis of obstruction	Adhesions	Yes
22576	75	?	No evidence of obstruction	Obstruction 30 cm from ileocecal valve fluid above obstruction	Yes
37900	63	Yes	Small bowel obstruction	Adhesions	Yes
2036	65	No	Partial obstruction	Adhesions	Yes
53671	53	Yes	Dilated loops of small bowel	Adhesions	Yes
54165	66	No	Small bowel obstruction	Adhesions	Yes
47533	47	No	Small bowel obstruction	Adhesions	Yes
19915	18	Yes	Partial small bowel obstruction	Adhesions	Yes
50433	39	Yes	Obstruction near terminal ileum	Adhesions	Yes
30514	32	Yes	Small bowel obstruction	Adhesions	Yes
31010	55	Yes	Partial obstruction	Adhesions	Yes
50016	41	Yes	Partial small bowel obstruction	Adhesions	Yes
14221	30	Yes	Dilated loops of small bowel	Adhesions	Yes
46601	30	?	Films inconclusive	Adhesions	Yes
18920	24	No	Partial obstruction	Adhesions	Yes
10541	35	Yes	Small bowel obstruction near ileocecal valve	Adhesions adherent to fundus	Yes
11102	61	?	Small bowel obstruction	Adhesions	Yes
10504	83	Yes	Partial small bowel obstruction	Adhesions and gangrenous gut	No
5520	45	Yes	Small bowel obstruction	Adhesions	Yes
12082	48	Yes	Early partial small bowel obstruction	Adhesions	Yes
11768	54	Yes	Observed for 3 days Partial small bowel obstruction on final film	Adhesions	Yes
16191	73	No	Partial small bowel obstruction	Adhesions	Yes
20145	50	Yes	Small bowel obstruction	Adhesions	No
30403	71	Yes	Suggestive of small bowel obstruction	Adhesions	No
40326	24	Yes	Gas in small and large bowel, question of partial obstruction question of ileus	Adhesions under scar	No
2460	24	Yes	Partial obstruction, ileum	Adhesions to scar	No
50041	68	Yes	Intestinal obstruction	Adhesions	Yes
51432	68	No	Partial intestinal obstruction	Adhesions	Yes
4959	15	Yes	Intestinal obstruction	Loop adherent to McBurney incision	No
2483	13	Yes	Partial small bowel obstruction	Small intestine adherent to scar	Yes
51820	61	Yes	Intestinal obstruction, small bowel	Adhesions to wall in region of old scar	Yes
26185	42	Yes	Intestinal obstruction	Pelvic adhesions	No
51306	37	Yes	Partial intestinal obstruction	Pelvic adhesions	Yes
6188	46	Yes	Partial small bowel obstruction	Multiple adhesions	Yes
36951	79	?	Small bowel obstruction	Adhesions bands	No
50889	28	Yes	Ladder formation Small bowel obstruction	Adhesions bands	No
19410	17	Yes	Partial small bowel obstruction	Adhesions, bands	Yes
20634	31	?	Partial small bowel obstruction	Adhesions, bands	Yes
110	33	?	Partial small bowel obstruction	Adhesions, bands	Yes
5173	46	Yes	Hairpin loop indicating obstruction	Adhesions bands	Yes

4 The importance of taking a "scout film" first and special views as necessary, depending on the history, physical findings, and the first film, is stressed

5 The anatomy of the small bowel is discussed in relation to the radiographic changes

Maine General Hospital
Portland 4 Maine

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DISCUSSION

Arthur J Present, M D (Tucson, Ariz) Excluding fractures, there is probably no x-ray emergency which calls us to the office more frequently than acute intestinal obstruction There is certainly no emergency in which our services can be more helpful if we are careful in the manner in which we study the cases I hope that our results can be as good as those of the essayists, who are to be complimented

The radiologist has an opportunity to be helpful in a critical situation and therefore a thorough roentgen study is indicated Not only must he obtain films adequate from a technical point of view but he cannot rest on the wet film diagnosis where he frequently finds himself cornered for an opinion

It cannot be over-emphasized that *all* the information on a film should be considered We can frequently find indications as to the level or the source of the obstruction from minute details, not always as clear-cut as the gallstones which we have seen demonstrated I think the careful survey of the abdominal film is most important to exclude the possibility of free gas in the peritoneal cavity as evidence of perforation following obstruction, since that is undoubtedly the most serious complication

We have found that the initial examination, no matter how careful, is often not adequate—which suggests decubitus films, upright films, and flat films—but we must examine the patient frequently in order to find the source or the level of obstruction, or even to confirm its presence.

I should like to emphasize the fact that, even though it causes considerable discomfort, we have often found it useful to turn our patient over, for prone films, thus obtaining considerable information as to the caliber of the involved bowel and also a compression effect We have also had success frequently by decompression and re-examination

The last thing I should like to say is that we have been fooled—and I am sure others have been—by a normally functioning colon in the presence of small bowel obstruction That warning I hand on because we have seen perfectly normal bowel movements in the presence of obstruction

SUMARIO

Diagnóstico Temprano de la Obstrucción Aguda del Intestino Delgado

Al estudiar 100 casos de obstrucción del intestino delgado y correlacionar los hallazgos operatorios y roentgenológicos, los últimos resultaron terminantes en cuanto a la presencia de obstrucción en 95 por ciento de los casos La radiografía permitió localizar el nivel de la obstrucción ciego, íleon, mitad del intestino o íleon

Recálcase la importancia de obtener primero una película "exploradora" y vistas especiales conforme a las indicaciones derivadas de la historia, los hallazgos físicos y la primera película

Se discute la anatomía del intestino delgado en relación con las alteraciones radiográficas

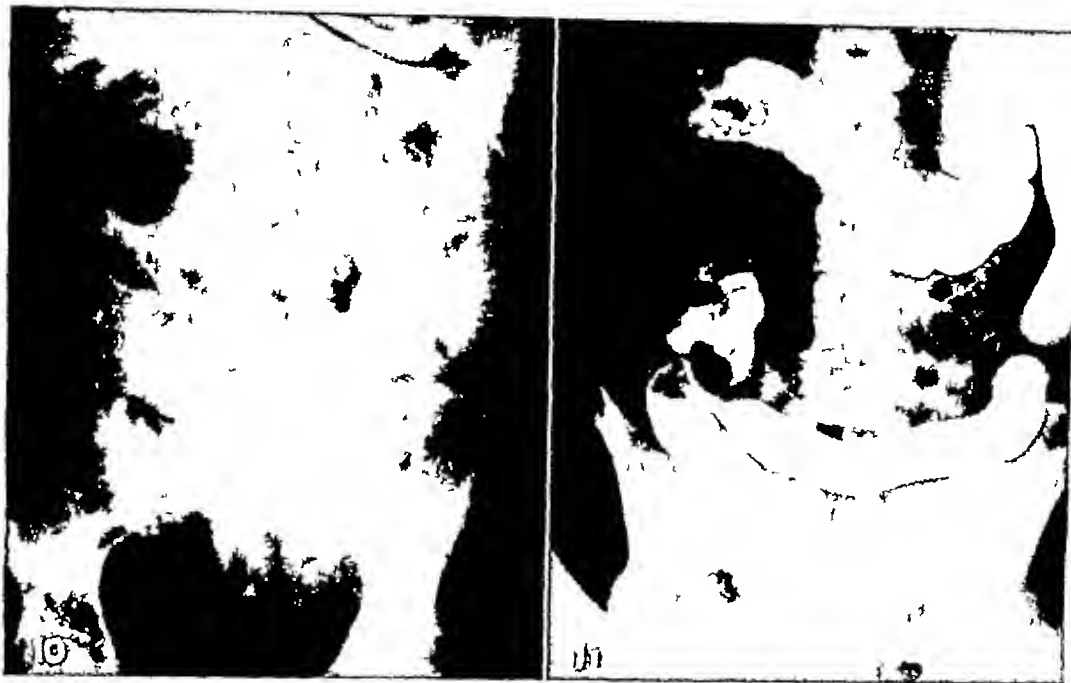


Fig. 10 Dilatation of the small and large bowel. The segment in the right lower abdomen has the appearance of colon.

Fig. 11 Same case as Fig. 10. A barium enema study demonstrated the sigmoid in the right lower quadrant and a markedly dilated cecum. Operative findings demonstrated a volvulus of the cecum and also obstruction at the terminal ileum.

DISCUSSION

It must be emphasized that there are a large number of cases presenting problems in the diagnosis of obstruction that will require frequent examination of the abdomen, including palpation and auscultation as well as repeated radiographic studies. The selection of cases that have been verified surgically necessarily limits the doubtful cases and allows for a more accurate correlation of the roentgen and operative findings.

In this series the radiographic findings were accurate in 94 per cent of the cases. In addition, in 50 cases in which the point of obstruction was stated in the operative notes, operation and the radiographic findings accurately located the level.

Always it should be stressed that, important as they may be, the roentgen findings are only an adjunct to the history and physical examination and other laboratory data. All should be correlated before

TABLE III. MECHANISM OF OBSTRUCTION. ANALYSIS OF 100 CASES OF SMALL BOWEL OBSTRUCTION

Adhesions with previous laparotomy	55
Adhesions without previous laparotomy	15
Adhesions previous operation not stated	8
Internal hernia	8
Meckel's diverticulum	3
Gallstones	3
Lipoma (causing intussusception)	2
Intussusception (one due to carcinoma of cecum)	2
Adhesions due to carcinoma not diagnosed previously	1
Tuberculous ileitis	1
Terminal ileitis	2
	<hr/> 100

coming to a definite conclusion as to the final diagnosis.

SUMMARY

1 One hundred cases of obstruction of the small intestine were studied and operative and roentgen findings correlated.

2 The radiographic findings were conclusive of obstruction in 94 per cent.

3 The level of obstruction can be localized roentgenographically, i.e., jejunum, mid bowel, or ileum.

4 The importance of taking a "scout film" first and special views as necessary, depending on the history, physical findings, and the first film, is stressed

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Treatment of Epitheliomas of the Skin¹

THEODORE P EBERHARD, M.D

Jefferson Medical College and Hospital, Philadelphia, Penna

THE POTENTIAL high curability of basal-, squamous-, and basosquamous-cell epitheliomas of the skin is generally accepted, but there is a singular lack of unanimity of opinion as to the best means of achieving results. This paper presents the procedure which was worked out and used in the treatment of these tumors at the Ellis Fischel State Cancer Hospital, Columbia, Mo., and a statistical analysis of the results obtained in 492 patients treated there between September 1939 and September 1942.

One assumption forms the basis of the rationale of the method, namely, that either radiation or surgery, properly used, can cure any of these lesions. The support for the assumption lies in the large number of articles reporting almost equally good results from the use of each method. The widely varying techniques of irradiation used by different workers, all again claiming favorable results, also indicate that there is little or no difference in radiosensitivity between the three types of tumor. The conclusion is that the histology of a lesion is no criterion for the choice of treatment. Rather should one base his selection upon the size and location of the growth, using that method which can be most effectively employed, which will give the best cosmetic result, and impose the least hardship upon the patient.

Inasmuch as this deduction holds good for almost no malignant skin tumors except the epitheliomas, accurate diagnosis is necessary. This can be established only by biopsy, and that procedure was carried out on all of the cases in this series.

The size of an epithelioma is the first factor to be considered in determining treatment. If it is less than 3 mm in diameter, an adequate biopsy will remove practically

all of the tumor. If the location of the lesion presents no contraindication to extension of the excision for another few millimeters, immediate excision should be done. It should, perhaps, be emphasized that in these instances the pathologist bears a responsibility for more than the diagnosis, he must examine the specimen in such a way as to determine whether the growth has been actually completely excised. If it has, there is no necessity for any further treatment. If not, re-excision or irradiation must be carried out. At the other extreme from these tiny lesions are the extremely large ones. Here, the combined knowledge and judgment of the radiologist and the surgeon may be taxed to the limit. These cancers have always destroyed large amounts of tissue and have usually involved bone. Bone invasion makes permanent arrest by radiation extremely difficult, if not impossible. On the other hand, complete removal of the lesion by surgery may mean creation of an irreparable defect which is incompatible with essential function or with life itself. In such a case, of course, one should attempt as much as can be accomplished with radiation and hope that the arrest will last for the duration of the patient's life. When surgical removal and plastic repair can be done, this is the method of choice, whether or not there is bone involvement, for tissues already damaged by radiation are unsatisfactory for reparative surgery, and radiation will not fill in a deficiency caused by the tumor itself. Epitheliomas of medium size, from 0.3 cm to 3.5 cm, leave the physician free to choose that form of treatment which will give the patient the best cosmetic and functional result, and often allow him to consider even such items as convenience and expense.

¹ Presented at the Thirty second Annual Meeting of the Radiological Society of North America Chicago Ill Dec 1-6, 1946

The location of the lesion usually provides the most important criterion. A few general rules may be briefly stated. If radiosensitive, important, contiguous structures cannot be protected, radiation is contraindicated. A narrow scar is preferable to a round, blanched area, but radiation, properly done, can usually produce results superior to those achieved by skin grafting of any type. The eye presents an excellent illustration of how important a matter of a few millimeters difference in location may be. When the tumor lies upon the bulbar conjunctiva or deep in the conjunctival fold, it is impossible to shield the globe and retrobulbar fat. Very small lesions in these locations can often be excised without damaging the eye, and the prosthesis employed immediately after enucleation of the eye for larger growths gives a far better appearance than a shrunken, heavily irradiated eye. The immediate treatment and post-treatment discomfort is also less with surgery. On the contrary, even tiny excisions along the lid margins produce defects. With the proper use of subpalpebral lead shields, growths of considerable size may be safely irradiated without damage to the eye and with little or no ultimate defect in the contour or function of the lid. At the canthi, surgery will almost inevitably destroy either the lacrimal gland or duct, both of which can usually be preserved by the use of radiation. On the hand, too, with its thin layer of tissue over the tendons and bones, slight differences in diameter or depth of lesions may lead to opposite decisions as to therapy. Only by the close collaboration of the surgeon and the radiologist can the basic rules be correctly applied to the multitudinous situations offered by individual cases.

In many instances, of course, neither size nor location forces a decision. The particular skills of the readily available practitioners may be of importance. The relation of the treatment schedule to the patient's daily routine sometimes may be allowed to dictate the course to be followed. Expense may also be of importance, for,

while an ethical physician will always adjust his fee to the patient's means, there are certain ancillary costs which are not so flexible and which may prohibit one or another form of treatment.

Metastases should be treated by radical block dissection whenever possible. It is perfectly true that metastatic nodes may sometimes be controlled by radiation, but the percentage of successful results is considerably lower than when surgery is employed. The treatment must be intensive, resulting in severe radiation fibrosis of the treated area. In most instances, the node therapy should be entirely separate from that of the primary lesion and should be deferred. There are several reasons for this. The infection occurring in ulcerated carcinomas often gives rise to palpable nodes. It also complicates real node metastases. Thus, if the primary lesion is healed first, all node dissections become safer, and many contemplated operations will be found to be unnecessary. Finally, the futile treatment of metastases when the primary lesion cannot be controlled will be avoided.

Recurrent, or more properly persistent, primary lesions should usually be treated by some other method than the one originally employed. Those which persist after surgery usually do so because they are diffuse, infiltrating tumors the complete removal of which involves the excision of undue amounts of tissue, those still present after radiation are presumably radio-resistant.

RADIATION TECHNIC

There is a strong tendency among radiologists to use large individual doses in the treatment of cutaneous epitheliomas. Many even resort to the single massive dose technic. This is understandable, for it is often difficult to convince the patient that daily treatments for two weeks are for his benefit and not simply to enrich the pocket of the radiologist. But it is not defensible. These tumors are cancers, and there is no more reason to disregard the teachings of Coutard in regard to protract-

tion and fractionation than if one were dealing with a carcinoma of the larynx. A large percentage of long-term arrests, better cosmetic results, and fewer necroses will reward the patience of the careful therapist.

The kilovoltage should vary with the thickness or depth of the lesion. Most of the cases in this series were treated with 120 kv and 140 kv. Lower voltages than these are safe only with the most superficial tumors, and the deep-tissue damage of 200 kv is necessary only with the very deep ones. Additional filters from 3 mm Al to 0.5 mm of Cu were used with the appropriate kilovoltages, the machines all having inherent filtrations of 0.25 mm Cu equivalent. The target-skin distances varied from 25 cm to 50 cm depending upon the thickness of the tumor and the kilovoltage. The fields were limited by means of cones and individually fitted lead cut-out shields. Around the eye, silver-plated lead shields were used under the lids and cut-outs over the outer surfaces.

At first, daily doses of 300 r and 400 r were used, but later experience showed that these were too high to give good cosmetic results with any but the smallest fields, and they were reduced. The final ordinary routine called for 200 r per day for the first 1,600 r, 300 r per day for the next 1,200 r, and 400 r per day for the last 800 r. These dosages varied with the size of the field, the kilovoltage, and the total dosage to be given. Some of the smallest tumors received as high as 5,000 air roentgens and a few of the very large superficial ones as little as 2,500 r. The aim should be always to get at least 3,000 tissue roentgens into the depth of the tumor.

Nearly one-third of the lesions were treated with interstitial radium. When hospitalization can be easily accomplished, this method has several advantages. From a theoretical standpoint it should be ideal, for it places the highest intensity of radiation at the growing base and edge of the tumor. Its rapid decrement of intensity can sometimes be used to advantage as a means of protecting underlying structures

TABLE I TYPES OF LESIONS AND AGE OF PATIENTS

Patients	492
Lesions	760
Basal-cell	545 in 367 patients
Squamous cell	197 in 154 patients
Ba-squamous-cell	18 in 17 patients
Age	
Mean	70 years
Median	72 years

which cannot be shielded from direct external rays. Most important of its features is the saving in time. This may be extremely important for out-of-town patients, who may be treated in a matter of twenty-four hours with equally good therapeutic results and almost as good cosmetic results as would be accomplished with two weeks of x-ray therapy. Needles containing 3.3 mg of radium per centimeter of active length or 5 mg per cm were used, the former taking an average of forty hours' treatment instead of the twenty-four hours required with the higher intensity. All of the needles had walls of 0.5 mm of gold or platinum. Surface applicators were never used, because of the numerous difficulties involved in making and applying them and the absence of any therapeutic advantages.

The surgery was done exclusively with the cold knife. Neither cautery nor the "electric knife" was used. Cautery destroys the specimen and also makes it impossible for the operator to know the depth to which he has gone. The round white scars are as bad as the worst radiation scars. The "electric knife" chars the tissues slightly, distorts the cell structure of the specimen, and again makes for unnecessarily prominent scarring. The supposed cancericidal action of the heat does nothing but give the operator a false and misleading sense of security.

STATISTICAL ANALYSIS

The mean age of the patients was seventy years and the median age seventy-two years (Table I). This is almost ten years older than the patients in most other series and accounts for the large number of deaths from intercurrent disease. Treatment facilities having been brought to the indigent rural population for the first time with the

TABLE II ANATOMICAL DISTRIBUTION OF LESIONS

Location	Basal-Cell	Squamous-Cell	Baso-squamous-Cell
Scalp	6		
Forehead	20	7	1
Nose	108	14	4
Ala nasi	17		
Cheek	183	88	4
Upper lip	5	1	
Lower lip and chin	20	4	
Upper eyelid	11	1	
Lower eyelid	20	2	
Inner canthus	21	3	
Outer canthus	8	1	
Conjunctiva			1
Ear, pinna	27	27	3
Neck	59	20	5
Trunk	18		
Arms	8	2	
Wrist		2	
Hand and fingers	2	14	
Legs	3	2	
	545	197	18

opening of the hospital, the proportion of far advanced, often hopelessly advanced, lesions received during the first year was discouragingly high. Later material approximated in quality that seen in most large clinics. Forty-six patients had more than one kind of lesion, and 139 had multiple lesions of the same kind. The anatomical distribution of the lesions is detailed in Table II.

The final results of the whole material are shown in Table III and of the basal- and squamous-cell lesions separately in Table IV. The figures in the second column of Table III and the second and fifth columns of Table IV are absolute percentages. Those in the third and sixth columns are calculated. Various schemes have been proposed to adjust the cure rate in skin tumors to compensate for the high

percentage of loss from intercurrent disease before the end of the follow-up period, and thus to bring the figures more nearly into line with the computed cure rates of cancer occurring in the earlier decades of life. Magnusson (1) chose to apply his known recurrence rate to the number of patients dying of intercurrent disease, counting the resultant number as dead of disease and adding the remainder to his known "living and well." Warren (2) objects to this use

TABLE III THREE-YEAR RESULTS FOR ENTIRE SERIES

	No Patients	Percentage of All Patients	Percentage of Survivors (Calculated)
Living free of cancer	327	60.4	88.6 (W) 83.3 (M)
Living with cancer	5	1.2	
Dead of cancer	43	8.7	
Lost to follow up	28	5.6	
Dead of other diseases, free of cancer	80	18.1	

of hypothetical cures. Instead, he applies the current general mortality rate for a population of the same age group to his total number of patients and computes his final cure rate upon this number of calculated survivors instead of upon the original number of patients in the series. Both methods have been used here and the results entered with the letters M and W in parentheses. Curiously, higher computed rates are obtained in this series by means of Warren's method than with Magnusson's.

In Table V the results, both absolute

TABLE IV THREE YEAR RESULTS FOR BASAL CELL AND SQUAMOUS CELL LESIONS

	Basal Cell			Squamous Cell		
	No of Patients	Per Cent	Per Cent of Survivors (Calculated)	No of Patients	Per Cent	Per Cent of Survivors (Calculated)
Total	307	100		154	100	
Living free of disease	235	64	85.6 (W) 87.2 (M)	92	59.7	80.9 (W) 75.3 (M)
Living with disease	3	0.8		2	1.3	
Dead of disease	18	4.9		25	16.2	
Lost to follow up	10	5.2		9	5.8	
Dead of intercurrent disease	00	0.0				

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DISCUSSION

J A del Regato, M D (Columbia, Mo) After listening to Dr Eberhard, one cannot but be captivated by his logic. I have examined and followed hundreds of patients treated by him at The Ellis Fischel State Cancer Hospital, and consequently I have had an unusual opportunity to appreciate his excellent results in the treatment of carcinomas of the skin.

I agree with Dr Eberhard that the histologic character of carcinomas of the skin does not offer a basis for choice of treatment. I would like to add, specifically, that the reputed radioresistance of the *adenoides cystica* type of carcinoma is a myth. I also agree that invasion or proximity of cartilaginous or bony structures is not a contraindication to radiation therapy, but only a circumstance requiring special adaptation of technic. I also agree that surface curietherapy has no special virtues, but, unlike Dr Eberhard, I extend the same consideration to include the interstitial application of radium. There can be no question as to the ability to control carcinomas of the skin by skillful interstitial curietherapy, but the cosmetic results can be improved and a number of cases of radiodermatitis avoided when adequate roentgen therapy is substituted.

We hold the opinion that adequate roentgen therapy is the treatment of choice of carcinomas of the skin, the size of the lesion and its location will determine the quality of radiation needed, the maximum daily dose administered, and the required protraction. The minimum total dose which is necessary to sterilize the tumor will vary with the size of field, the quality of radiations, and the average daily dose. This implies a diversity of techniques to be applied to the different cases and forbids routine methods. We give preference to surgical treatment in certain instances where it accomplishes effectively and expeditiously what would require more time and attention by means of roentgen therapy. Lesions of moderate size of the skin of the cheeks and cervical regions may be widely excised without disfigurement, carcinomas of the scalp and dorsum of hands are very adequately treated by excision and skin grafts. In general surgical treatment is most practical in the rare carcinomas of unexposed areas of the skin. That we give preference to the surgical treatment of these lesions does not mean that roentgen therapy is contraindicated. The surgical treatment of carcinomas of the dorsum of hands by excision and skin graft is very satisfactory, but when the surgical excision implies mutilation roentgen therapy should be first considered. Very often the clinical assumption of invasion of tendons of the hand is not verified on microscopic examination of the surgical specimen. The adherence in depth and resulting dysfunction is more often due to underlying inflammation (Ackerman). In such cases an amputation may not be justified and protracted

roentgen therapy is the treatment of choice. In the treatment of carcinomas of the eyelids, of the inner and outer canthus of the eye, of the skin of the ear, of the preauricular and retroauricular regions, of the skin of the nose, and of extensive lesions everywhere, the suppleness of roentgen therapy, its adaptability to the peculiar requirements of the lesion or of the region, cannot be excelled by any other method.

In the present state of our development in the treatment of cancer, a skillful performance is often more important than the choice of method. I am in complete agreement with Dr Eberhard in respect to the results obtainable by roentgen therapy. But, although I am witness of the excellent results which he has obtained with interstitial curietherapy, I feel that I would be incapable of reproducing these results by the same means, and I remain convinced of the universal virtues of roentgen therapy in carcinomas of the skin.

Henry J Ullmann, M D I am interested particularly in these statistics of curability, for I think I shall have to go back and review the cases that I reported before this Society about two years ago, and which were published in *RADIOLOGY* (46: 279, 1946) within the last year, on a comparable number of lesions with a somewhat higher percentage of good results. In my locality I get a higher percentage of patients in the lower age group. I have quite a number in the forties, and they are common in the fifties. Of course, in Southern California we have a fairly dry climate and considerable sunlight. I have treated the majority of my cases with roentgen rays and a few with radium.

I concur heartily with the warning that it is extremely dangerous to treat over bone, especially over the hands and wrists. I have had some unfortunate results in these areas with radiation of any type. On the scalp I usually treat by surface applications of radium with heavy filtration, and with the applicator fairly close to the lesion to reduce the depth dose and injury to the underlying bone. The results of this method have been very satisfactory. I should hesitate to use the roentgen ray with what I call a cauterizing dose on the scalp.

Theodore P Eberhard, M D (*closing*) I must apologize first for having somehow or other missed Dr Ullmann's paper in my review of the literature.

On the matter of late radiation necrosis, I think that further analysis of this series, which I did not have time to complete, will show a considerably lower percentage than Dr Ullmann mentioned, and that is one of the reasons that I believe in this type of therapy. The multiple series type of treatment I believe is what contributes to the later necrosis.

TABLE V THREE-YEAR CURE RATES, COMPARED WITH RESULTS AT RADIUMHEMMET

	Three Year Cure Rates		Calculated Three Year Cure Rates	
	Our Series	Radium hemmet	Our Series	Radium-hemmet
Whole material	66 4	73 6	83 3	86 0
Basal-cell	64 0	81 6	87 2	93 2
Squamous-cell	59 7	60 1	75 3	77 5

and computed, are compared with Magnusson's figures from Radiumhemmet, Stockholm. After adjustment for the higher losses from intercurrent disease in our series, there are no statistically significant differences.

The relative merits of several forms of treatment can be compared on a survival basis only if each treatment has been applied indiscriminately to consecutive cases and if the disease is one which carries a high direct mortality. Such is not the case in this series. The methods of treatment were carefully selected according to the criteria just described. Secondly, these epitheliomas cause death directly only after extremely long periods of neglect, and even then only in a low percentage of the patients. Recurrence, on the other hand, will inevitably occur if the treatment is improper, and 95 per cent of the recurrences will be apparent within three years. Table VI shows the recurrence rates for all

TABLE VI COMPARISON OF RECURRENCES WITH THREE METHODS OF TREATMENT

Therapy	Basal cell, No Cases		Squamous cell, No Cases	
	Re currences		Re- currences	
X ray	333	17 (5 1%)	97	4 (4 1%)
Radium	163	8 (4 9%)	72	3 (4 2%)
Surgery	49	1 (2 0%)	28	3 (10 7%)

three forms of treatment and for lesions of both major types. The basosquamous lesions were too few to have any significance and were omitted. It is immediately seen that there is no real statistical difference. The seemingly bad results from surgery of the squamous-cell lesions are il-

lusory. This group is small and contains 11 lesions of the hand and wrist, several of which had massive axillary metastases when first seen. Two of the three recurrences took place in the stumps after amputation in these cases.

SUMMARY

A treatment plan is presented for basal-, squamous-, and basosquamous-cell epitheliomas of the skin in which the choice of the method of treatment is based primarily upon the size and location of the lesion, secondarily upon the probable cosmetic result, and not at all upon the histology. Biopsy is advocated to insure that the lesion belongs in the epithelioma group. The size and location are considered important because they affect the efficiency with which radium, x-rays, and surgery may be used.

Seven hundred and sixty lesions were treated on 492 patients in three years. At the end of a minimum three-year follow-up period, 327 patients (66 4 per cent) were living free of disease and 89 (18 1 per cent) had died of other diseases. When Magnusson's correction factor for those dying of intercurrent disease is inserted, the cure rate becomes 83 3 per cent, which compares favorably with the Radiumhemmet rate of 86 per cent. The results of the three methods of treatment are compared by using the recurrence rate as the basis, and again no statistically significant differences are observed.

NOTE. I am deeply indebted to my friends and former colleagues at The Ellis Fischel State Cancer Hospital for permission to use this material and for their generous assistance in compiling the data.

Department of Radiology
Jefferson Hospital
Philadelphia 7, Penna

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A Grid-Front Cassette

A Useful Application of the Stationary Grid

JOHN D. CAMP, M.D.

Section on Roentgenology, Mayo Clinic, Rochester, Minnesota

SINCE THE introduction of the stationary grid for roentgenographic purposes, roentgenologists have found the device useful in circumstances in which a conventional Potter-Bucky diaphragm cannot be employed. The use of the stationary grid in many instances, however, has been complicated by a difference in the size of the grid unit and the various cassettes available. When the grid is used in the vertical position, various makeshift devices, such as sandbags, adhesive tape, clips, etc., have been necessary to hold the grid in apposition to the cassette.

To overcome this difficulty and obtain a grid-cassette combination that could be placed quickly in all positions, it was felt that the grid should be an integral part of the front of the cassette. This was achieved by removing the bakelite front of a Picker cassette and replacing it with a metal Lysholm grid cut to corresponding size. The front of the metal Lysholm grid was protected by a thin bakelite or plastic sheet. Because of the thinness of the Lysholm grid, the combined thickness of the grid and protective sheet was the same as the bakelite front that had been removed. The result was a grid-front cassette which was the same size in all dimensions as a conventional cassette (Fig 1). This combination has many advantages that are readily apparent. The detail of the resulting roentgenogram is improved, the shadows of the grid lines are narrower because of lessened distortion, and the cassette because of its standard size can be used in any cassette tunnel or stereoscopic shift device.

A similar grid front cassette has been made for use of the roentgenologists at the

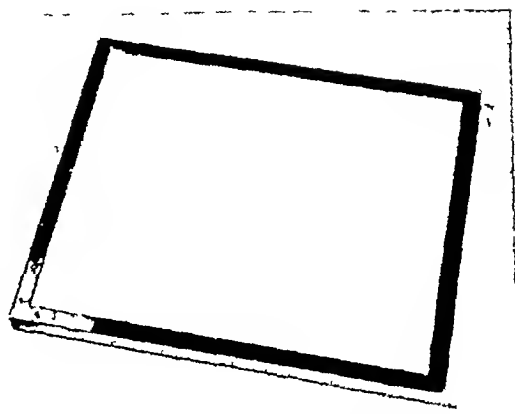


Fig 1 Grid-front cassette. A metal Lysholm grid and protective plastic covering have been substituted for the conventional bakelite front of the cassette. The resulting grid-cassette unit is of the same size and thickness as the original cassette.

Mayo Clinic by replacing the bakelite front of a standard Kelley-Koett cassette with a Liebel-Flarsheim stationary grid and protecting bakelite front¹. The result was a unit similar to that first mentioned but about 1/8 inch (0.32 cm) thicker than the standard cassette. This disadvantage can be eliminated by a slight change in the design of the cassette. Any other cassette likewise can be adapted to this purpose. Because of the difference in construction of the Lysholm and Liebel-Flarsheim grids, there is a difference in the quality of the resulting roentgenograms that in my experience favors the metal grid.

My colleagues and I have used these grid-front cassettes for nearly a year and are frequently finding new applications for them, since they can be made in any standard size. They have become indispensable for bedside examination of structures that normally would require a Potter-Bucky diaphragm. Excellent bedside roentgeno-

¹ Since this article was prepared, I have been informed that Dr. James P. Rousseau of Winston-Salem, N. C., utilized a special Liebel-Flarsheim grid front cassette for examinations of the hip several years ago.

Dr Ullmann I use the long-protracted procedure only with the higher voltage. The time is three weeks with the copper filter. I take only a week with the lower voltage.

Dr Eberhard I agree to higher voltages for the thicker lesions. I seldom go down to 100. I think the failures result from too low voltage, underestimating the thickness of the lesion.

SUMARIO

Tratamiento de los Epitelomas Cutáneos

Preséntase un plan terapéutico para los epitelomas baso-, escamo-, y basoesquamosocelulares de la piel, en el cual la elección del método de tratamiento se basa primordialmente en el tamaño y localización de la lesión y secundariamente en el probable efecto estético, sin tomar en cuenta la histología. Se recomienda la biopsia para cerciorarse de que la neoplasia pertenece al grupo epitelomatoso. El tamaño y la situación se consideran importantes por afectar la eficacia con que pueden utilizarse el radio, los rayos X y la cirugía.

En tres años tratáronse 760 lesiones en 492 enfermos. Al cabo de un periodo mí-

nimo de tres años de observación subsiguiente, 327 enfermos (66.4 por ciento) se hallaban vivos y sin enfermedad y 89 (18.1 por ciento) habían fallecido de otras enfermedades. Al aplicar el factor de corrección de Magnusson para los que mueren de afección intercurrente, el coeficiente de curación pasa a 93.3 por ciento, que se compara favorablemente con el 86 por ciento del Radiumhemmet. Al comparar el resultado de los tres métodos terapéuticos, tomando como base el índice de recurrencias, tampoco se observan mayores diferencias estadísticas.



EDITORIAL

A Total Population Chest Survey

In view of the importance to radiologists of the proposed campaign of the National Tuberculosis Association urging every one in the United States to have an x-ray examination of the chest, RADIOLOGY has deemed it expedient to publish, with a few minor omissions, the following correspondence between Dr Francis J Weber, Medical Director Chief, Tuberculosis Control Division, U S Public Health Service, and Dr L Henry Garland, President-Elect of the Radiological Society of North America

WASHINGTON 20, D C
Aug 20, 1947

Dr L Henry Garland
450 Sutter Street
San Francisco 5, Calif

DEAR DR GARLAND

As you may know, the National Advertising Council has accepted the proposal advanced by the National Tuberculosis Association to put on a campaign starting after the first of the next calendar year urging the people of this country to have chest x rays. The proposal was accepted because it was the feeling of the Advertising Council that specific action could be urged on the public, leading toward ultimate public benefit.

The advertising agency selected to handle the preparation of the material is now at work. The National Tuberculosis Association and the United States Public Health Service are serving as sponsoring consultants to this agency. It is planned that the final material will urge the public to consult physicians, tuberculosis associations, and health departments with respect to obtaining chest x rays. This general material will be supplemented by material which can be adapted to local area use so that programs as developed locally may tie in with the national campaign. The National Tuberculosis Association at its last annual Board meeting voted to underwrite the preparation of the materials.

It is hoped that this campaign will receive the active support of the medical profession particularly the organized groups such as the Radiological Society of North America, the American Roentgen

Ray Society, the American Medical Association, as well as the two groups specifically interested in diseases of the chest, the American Trudeau Society and the American College of Chest Physicians.

If this concept of an approach to the public on a public health problem is consistent with your thoughts, I should like to enlist your active support of the program among the officers and members of the professional organizations.

Particularly, you can do much to advance the program because of your position of recognized leadership in your field, as shown by your election to the presidency of the Radiological Society of North America.

Sincerely yours,
FRANCIS J WEBER

SAN FRANCISCO 5, CALIF
Aug 28, 1947

Francis J Weber, Medical Director
Chief, Tuberculosis Control Division
U S Public Health Service
Washington 25, D C

DEAR DR WEBER

This will acknowledge your letter of Aug 20.

Several years ago, the American College of Radiology, in formally approving the principle of mass chest surveys for the detection of pulmonary tuberculosis, emphasized that "Films should be examined by physicians who are trained and competent to interpret radiographs of the chest."

Frankly, this appears to be the crux of the problem. You state that the National Tuberculosis Association will urge all persons to have "chest x rays" which may mean nothing. Having a chest x ray is valueless unless it is properly interpreted.

How and where should we direct persons so that they may receive a reliable x ray examination?

Should we urge them to be examined by qualified physicians in their offices?

Should we direct them to certified radiologists (names are obtainable from most local county medical societies)?

If directed to other than certified radiologists, should we set up standards to protect the public? A chest x ray at a Tuberculosis Unit or a Public Health Depot may be read by an unknown reader, qualified or otherwise. Should we insist on tested readers for all survey centers, mobile units, etc?

grams of the skull, chest, spinal column, pelvis, urinary tract, etc., are now easily obtained. In the operating room the grid-front cassette has proved most desirable in the examination of fractured hips and for cholangiograms. It is used routinely for certain projections during encephalography, ventriculography, and other special examinations. Since the grid-cassette unit may be used in any cassette shifter, it permits the production of roentgenograms of the Potter-Bucky type when a high-speed vertical type of Bucky unit is not available. For special examinations, such

as arteriography, angiocardiology, and others in which a rapid sequence of exposures is desirable, the use of the grid-cassette unit eliminates the time lag that occurs when the conventional Potter-Bucky mechanism is employed.

A disadvantage of the grid-front cassette is its relatively high cost, however, others who have had an opportunity to use the device have stated that its usefulness more than compensates for that.

Section on Roentgenology
Mayo Clinic
Rochester, Minn

SUMARIO

Chasis con Rejilla por Frente

Quitándole el frente de bakelita a un chasis o cassette y reemplazándolo con una rejilla y recubrimiento plástico como resguardo, se ha obtenido un chasis-rejilla del mismo tamaño y espesor que el primitivo y que ha encontrado numerosas aplicaciones en radiografía.



Now as to a training program for interpreters In regard to this, let me say that I admire very much the plan that you, in conference with others, worked out sometime ago in San Francisco. It is too bad that this plan had to be curtailed as a result of the war. However, now that the war is over, I think such a thing could be taken up again, worked out so that it is practical for a large part of the country, and then publicized in the right channels to see that such a program is set up in as many places as possible. In this we will have to rely on the educational efforts of societies like yours, because (frankly) we do not have the personnel or the funds with which to conduct a nationwide program of that type. We realize it is something to be done, however, and it seems that the best that should be done at this time would be to start it in one or two areas like yours, determine the most practical way of going about it, and attempt to get the funds from some place to make it possible to have similar programs in different parts of the country. One way to do it, for example, would be for the roentgen ray societies to get together with, let us say, the Medical Section of the National Tuberculosis Association, namely, the Trudeau Society, and work out some program much like the present post-graduate type of conference being held at different parts of the country. This is something which I feel such professional groups can do better than we ourselves who are in official work, although we are in a position to help such groups organize it and even do some of the work. Certainly we are anxious to help.

With regard to the possibility of postponement of the proposed advertising campaign, I feel sure that plans are too well advanced to consider such a move. As a matter of fact, the Council wanted to go ahead last year but were deliberately discouraged. It was decided to go ahead, however, this next January, with the program to begin quite slowly at first, the full effects not to be felt for several months. Therefore, there is still nearly a full year for planning, as well as an opportunity to observe the program and determine what the fresh demands of this new program will be.

This subject is such an important one that it would seem well if some of our staff could discuss this at your next annual meeting. At that meeting, I would hope to get not only the views of the Society regarding the desirability of this program from a control point of view but I would also like the Society's assistance in developing some workable plan by which we could better handle an increased load of routine x rays that might result from this advertising program. I think if we start in now, sound plans can be laid for the future. I might say that the Advertising Council will consider renewing the drive at the end of the next calendar year should the first year's efforts promise success. Therefore as you see, we actually have the time to plan the

things which you have suggested in your letter. Certainly we will want to work as closely as possible with such an important public spirited group as yours and I hope it will be possible to follow through on my suggestion that it be taken up at your next annual meeting.

Sincerely yours,
FRANCIS J. WEBER

SAN FRANCISCO 8, CALIF
Sept 23, 1947

Francis J. Weber, M.D.
Tuberculosis Control Division
U. S. Public Health Service
Washington 25 D. C.

DEAR DR. WEBER:

Thank you for your letter of Sept. 12th. After consulting with several radiologists throughout the United States, it is still our opinion that the best way of achieving the goal of a total population survey would be to set up a sound procedure first, and then to publicize it. In any event, most radiologists would welcome specific assurance of the U. S. Public Health Service and the National Tuberculosis Association on the following points:

1. Only qualified personnel will be used to supervise the technical procedure and make the interpretations of the survey films. Each county medical society will be asked to designate a list of qualified physicians who would be available in that district.

2. The U. S. P. H. S. and the N. T. A. will secure approval by each local county medical society before any survey center is established or utilized in this program.

3. A definite suggested procedure for the handling of cases which have abnormal shadows will be outlined, presumably with emphasis on regular medical and x-ray examination, sputum studies, and follow up.

We note in your recent letter that the proposed advertising campaign has been postponed once. Should not this be renewed in order that plans for correct procedure might be completed before the public is approached? As the London Letter to the J. A. M. A. (10-21-44) put it in part: "Anything that would weaken public confidence in mass radiography would impair its usefulness. So also would anything that would lead the public to expect too much from this method. Mass radiography has not made the diagnosis of pulmonary tuberculosis easier, on the contrary, it brings to light many symptomless cases. As the diagnosis of tuberculosis may involve change or loss of work and prejudice life insurance, it should be made only by persons with all the diagnostic procedures at their disposal."

Yours very truly,
L. HENRY GARLAND, M.D.

Should we notify them that (a) minimal pulmonary tuberculosis may be missed even on a large film and (b) that strictly speaking the diagnosis of tuberculosis always requires sputum confirmation? Therefore, such examination may also be required.

As long ago as 1941 the San Francisco Roentgen Society presented a proposal for a total population survey (for that city) to the San Francisco County Medical Society, the local Tuberculosis Association, and the Department of Health. An x-ray survey unit was set up in a central location and a significant number of the citizens have been examined to date. Owing to the war, the problem of testing readers had to be deferred. I regret to say that since return from service I have not yet been able to persuade the local tuberculosis or other officials to resume attempting its solution.

It would seem to me that the U. S. Public Health Service and the National Tuberculosis Association should first work out some simple and fairly reliable method of testing "readers" before embarking on any total population chest survey. This would tend to obviate what happened in one large county in California a few years ago: the local Tuberculosis Association conducted a mass chest survey on young persons and had the films read by local practitioners. The latter diagnosed some 40 per cent of the cases as positive for childhood tuberculosis! On having the films properly interpreted by two radiologists in Los Angeles this percentage was reduced virtually to zero. You are also doubtless familiar with the large western state in which some 35,000 miniature films were made a few years ago and were never read at all!

Would it be possible to postpone the proposed advertising campaign for some months in order that there might be set up suitable regional testing centers where potential film readers (internists, radiologists or others) might be tested? Further, in case survey units are employed, could you set up some method for technical supervision by certified radiologists so that the technical aspects of the program could be watched, and only films of the highest caliber produced? Sponsored by national authorities, supervised by certified radiologists and interpreted by tested readers you would have a mass chest survey which would really mean something. As Lanza observed (J. A. M. A., 63:30, 45), "Tuberculosis survey work should be conducted along medical lines, through a medical approach, and with interpretation by those who are capable of interpreting the films."

Preliminary to the above, some publicity concerning the program could be released. Perhaps the Report of the Council on Industrial Health of the A. M. A. on the question of mass health surveys could be reprinted and widely circularized (especially items 1 to 5—see J. A. M. A., 81:1, 45). Finally, to gain support of the medical profession at large, would it be wise to note that expert legal counsel has ex-

pressed the opinion that chest surveys involving as they do a diagnostic procedure, constitute the practice of medicine and should be treated accordingly?

These are knotty questions upon their fair solution, the success of the program may well depend.

Yours sincerely,
L. H. GARLAND, M.D.

WASHINGTON 25, D. C.
Sept. 12, 1947

Dr. L. H. Garland
450 Sutter Street
San Francisco 9, Calif.

DEAR DR. GARLAND:

I have your letter of August 28th and I wish at the very outset to thank you for it. This obviously well-thought-out missive of yours is an accurate presentation of the general problem of routine chest x-ray.

I also wish to acknowledge in the beginning, that there are no things in the picture you presented which are contrary to any views held by us. Actually we are in close agreement with all of your points and all that I can offer in reply is added explanation of how the advertising program came about and, at the same time, discuss some of the important things which led to our co-operation with the Council.

As you know, the Advertising Council is a non-profit group supported by the nation's industrial leaders and businessmen. It has no direct or indirect connection with the government and indeed pursues policies quite independent of any governmental agency. Since advertising has been so successful in many fields and inasmuch as it is really a part of our national life, these men through purely philanthropic motives feel that by placing this effective public instrument at the disposal of medical leaders it will be possible to use it in ways to promote better individual and community health. Since all of us as physicians have health conservation uppermost in our minds we felt very kindly to this offer.

While it is true that we can only proceed on a reduced scale at this time because of certain limitations which you have pointed out (limitations which are also appreciated by us) we still feel that much can be done as a start in this important field.

You will be interested in knowing that executives of this Council told me of formal requests from twenty different health organizations asking them to sponsor their respective health programs. After considering each one carefully they felt that the opportunities for doing good, even though limited as they are, would be best in an attack on tuberculosis.

It still remains to be answered as to how the program should be conducted, making certain that the best interests of the public are served. Here I think we should rightly insist, as you have emphasized, that chest films be interpreted only by those who are competent to interpret them.

Now as to a training program for interpreters. In regard to this, let me say that I admire very much the plan that you, in conference with others, worked out sometime ago in San Francisco. It is too bad that this plan had to be curtailed as a result of the war. However, now that the war is over, I think such a thing could be taken up again, worked out so that it is practical for a large part of the country, and then publicized in the right channels to see that such a program is set up in as many places as possible. In this we will have to rely on the educational efforts of societies like yours, because (frankly) we do not have the personnel or the funds with which to conduct a nationwide program of that type. We realize it is something to be done, however, and it seems that the best that should be done at this time would be to start it in one or two areas like yours, determine the most practical way of going about it, and attempt to get the funds from some place to make it possible to have similar programs in different parts of the country. One way to do it, for example, would be for the roentgen ray societies to get together with, let us say, the Medical Section of the National Tuberculosis Association, namely, the Trudeau Society, and work out some program much like the present post-graduate type of conference being held at different parts of the country. This is something which I feel such professional groups can do better than we ourselves who are in official work, although we are in a position to help such groups organize it and even do some of the work. Certainly we are anxious to help.

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ANNOUNCEMENTS AND BOOK REVIEWS

PENNSYLVANIA RADIOLOGICAL SOCIETY

At the 32nd Annual Meeting of the Pennsylvania Radiological Society, held May 9 and 10, 1947, at Pocono Manor, the following officers were elected to serve for 1947-48: Ralph D. Breton, M.D., Erie, President; Leslie H. Osmond, Pittsburgh, President Elect; George W. Chamberlin, M.D., Reading, 1st Vice President; William V. Dzurek, M.D., Pottsville, 2nd Vice President; James M. Converse, M.D., Williamsport, Secretary; Treasurer, Samuel G. Henderson, Pittsburgh; Editor, Paul G. Boyard, M.D., Trenton; Associate Editor, William I. Reilly, M.D., Clearfield; Editor Emeritus.

The 33rd Annual Meeting of the Society will be held at Erie, May 21 and 22, 1948, with headquarters at the Hotel Lawrence.

Books Received

Books received are acknowledged under this heading and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

TEMPOROMANDIBULAR ARTHROPATHY. By PER-MING NØRGAARD. A volume of 148 pages and 31 plates, with 132 figures. Published by Finis Munksgaard, Copenhagen, 1947.

Book Reviews

CANCER: DIAGNOSIS, TREATMENT, PROGNOSIS. By LAUREN V. ACKERMAN, M.D., Pathologist to the Ellis Fischel State Cancer Hospital, Assistant Professor of Pathology, Washington University School of Medicine, St. Louis, Mo., and JUAN A. DEL REGATO, M.D., Radiotherapist to the Ellis Fischel State Cancer Hospital, former Assistant to the Radium Institute of the University of Paris. A volume of 1,200 pages, with 749 illustrations, 42 in color on nine plates. Price \$20.00.

The authors of this new treatise on the subject of cancer are the pathologist and radiotherapist, respectively, in the State Cancer Hospital of Missouri, and the contents reflect their experience in the field of malignant neoplastic disease.

The book is divided into two parts, the first of which includes an introductory chapter, a chapter on Cancer Research by Dr. Michael Shumkin of the National Cancer Institute, and chapters on Pathology, Surgery, and Radiotherapy. This material is of a rather general nature and does not by any means encompass all of the available information on the subjects discussed. It does, however, constitute a good readable summary of important phases of the

cancer problem, furnishing a background for the later chapters.

Evidently through an oversight, the heading of Part II has been omitted, but this obviously begins with Chapter VI, on Cancer of the Skin, which is followed by thirteen chapters dealing with the other anatomical systems of the body and two final chapters on Hodgkin's Disease and Leukemia. The chapters are subdivided according to organs. In the chapter on the Digestive Tract, for example, there are sections on the esophagus, stomach, small bowel, appendix, large bowel, anus, salivary glands, pancreas, liver, gallbladder, and extrahepatic ducts and perianal region. Cancer in each of these sites is discussed under the further subdivisions: anatomy, incidence and etiology, pathology, clinical evolution, diagnosis, treatment, and prognosis, and this plan is followed throughout the book. Each chapter has its own list of pertinent references.

In their preface the authors are at some pains to explain the nomenclature which they have adopted. The word *cancer* at the heading of any chapter indicates that malignant tumors of different origin are included; *carcinoma* is used as a heading when only malignant epithelial neoplasms are considered, and the rarer tumors of the same area are treated in the section on differential diagnosis. Finally, the word *tumor* has been chosen as a heading whenever the frequency or the seriousness of the benign tumors, the difficulties of differential diagnosis of benign and malignant tumors, or the importance of the treatment which is indicated in either case justifies a joint consideration.

Dr. Ackerman and Dr. del Regato have filled a long felt need for a treatise not only on the general subject of cancer but one that contains authentic information on radiotherapy, a subject that too often has been disposed of in a few short paragraphs. The clinical descriptions and the pathologic studies will also be found helpful. This volume should prove of value to the student who is interested in cancer, and to the surgeon and radiologist who have a common problem in its management and cure.

OSTEOTOMY OF THE LONG BONES. By HENRY MILCH, M.D., Consulting Orthopedist, Maimonides Hospital, Attending Orthopedic Surgeon, Hospital for Joint Diseases and Riverside Hospital, New York, Fellow of the American Academy of Orthopedic Surgeons, the American College of Surgeons, and the New York Academy of Medicine. A volume of 294 pages with 181 illustrations. Published by Charles C. Thomas, Springfield, Ill., 1947. Price \$6.75.

For some years, Dr. Milch has described with enthusiasm the correction of deformities and the improvement of function brought about by altering

the shape and continuity of the long bones. Numerous exhibits at surgical meetings have testified to his interest and experience. He has now crystallized his past efforts into one readable volume which covers all details of the subject in an orderly manner.

Included in this work are the mathematical considerations and bases for correction of deformity by osteotomy. Special attention is given to preoperative plans to determine the proper amount of correction to be made, thus avoiding the pitfall of careless surgery. It is emphasized that an osteotomy requires precision and must be well planned in advance.

The discussion of upper extremity osteotomies, generally performed less frequently than osteotomy in the lower extremity, is a valuable part of Dr. Milch's book. Leg lengthening and leg shortening by osteotomy and epiphyseal arrest are considered at length. Of particular interest are the chapters dealing with types of hip and upper femoral osteotomies promulgated by various authors. Here the methods are outlined in detail, and their advantages and disadvantages are pointed out.

This book is not for the student or neophyte, but is an excellent volume for the orthopedist and is useful as a reference work to which one may turn for aid in the intelligent management of a difficult surgical problem. The more one uses osteotomies the more evident are their advantages in favorable cases. It is hoped that this work will popularize the use of this corrective procedure.

ACTIONS OF RADIATIONS ON LIVING CELLS. By D. E. LEA, M. A. Ph. D., Proflint Student of the Royal College of Surgeons. Formerly Fellow of Trinity College, Cambridge. A volume of 402 pages, with 83 tables, 4 plates and 61 figures. Published by Macmillan Company, New York, 1947. Price \$4.50.

The late D. E. Lea has written a much needed book but one whose scope is much more limited than the title implies. It is confined to the author's own interpretation of the target theory of the action of ionizing radiations on biological material. An introductory chapter deals with the physics of ionizing radiations giving useful calculations and tables on the dissipation of energy of x-rays, protons and alpha particles. The second chapter discusses chemical effects largely in terms of OH and H radicals produced. Although effects on enzymes are considered it is surprising to find no discussion of effects on proteins or organic and inorganic colloids, particularly since a considerable amount of work has been done with such systems and the results have been used in the interpretation of induced chromosome alterations to which a goodly portion of the book is devoted.

The target theory is developed in considerable detail. The methods for calculating target volume used by previous investigators are presented together with a more general method developed by the author

which is not subject to the limitations of the earlier procedures. Useful tables and graphs are given for calculating target size from dose-response data. Analysis of results with phage and virus in general agree with expectations from theory. However, although the fit is good in the case of alpha particles, it is poor with x-rays of 0.15 Å. The results with the larger phages may be explained by assuming that, unlike the viruses, they contain an appreciable amount of insensitive material and have a number of targets rather than a single one.

Induced rates of visible mutations per roentgen in virus, bacteria, and *Drosophila* are of the same order of magnitude, and are independent of intensity and wave length in the range 0.01–1.0 Å. However, at the w eye color locus the rate of induced mutation from wild type to w^x is 13 times greater than the rate for white eye to w^x , which the author does not discuss. In the production of mutations, neutrons are less efficient than x-rays, and alpha particles less efficient than neutrons. From these observations the author deduces that a single ionization suffices to produce a mutation. Dominant lethals are also discussed in relation to chromosome aberrations and evidence is furnished in support of the theory that recessive lethals are rejoined chromosome breaks.

By analogy with viruses, where the ratio of target to molecular size is known, the author computes the minimum gene size from the frequency of gene mutation per roentgen. From the relative efficiencies of x-rays, neutrons, and alpha particles in producing lethal mutations a gene target diameter of the same size (2–9 $\mu\mu$) is obtained. This is also the order of magnitude of the diameter of the chromosome sensitive volume obtained by methods not described by the author.

The greatest portion of the book is devoted to analysis of induced chromosome changes, but space will not permit a thorough discussion of the author's presentation and analysis. In developing his theory as it relates to chromosome aberrations, he has selected some sets of data and discarded others. Some times no reason for the selection is given, while in other cases data are discarded with a merely perfunctory statement which contrasts strangely with the thoroughness of the analysis in other portions of the book. The analysis and conclusions are based almost entirely on results obtained with *Tradescantia*. Chromosome exchanges are considered to vary as a function of the square of the x-ray dose and neutrons are found to be more efficient than x-rays in producing structural chromosome changes. Distinction is made between structural and physiological chromosome alterations and the relative neutron and x-ray efficiency for producing each, which fit the author's hypothesis but which to the reviewer seem entirely unsupported by the actual observations.

Exchanges are not at random, but analysis requires that exchange partners be separated by no

more than 1 micron. The number of until or primary breaks per roentgen calculated by three different methods is found to give good agreement. An alpha particle or proton passing through a chromatid will produce a break but only the end of the beta track has the same probability of producing a break.

Lethal effects in various organisms and inhibition of mitosis are also discussed.

In spite of such shortcomings as have been mentioned, this is a very stimulating and useful book. Much information from a variety of biological disciplines as well as from physics and chemistry has been assembled and interpreted in support of the author's thesis. The result in penetration as well as scope is a commendable achievement.

EL TORAX RADIOLOGICO DEL NIÑO EN LAS ENTERRADAS INFECTO CONTAGIOSAS. By RODOLFO I. TISCORNI, M.D. Roentgenologist of the Pedro Aycin Hospital of Montevideo, Uruguay. A volume of 115 pages with 37 illustrations. Published by Espasa Calpe, Argentina, 1945.

In this small volume, the author describes on the basis of a group of cases in children up to 13 years of age the roentgenologic aspects of the thorax in whooping cough, measles, diphtheria, influenza, typhoid fever, chickenpox, mumps, and scarlet fever. These descriptions are preceded by two introductory chapters and one dealing with the normal and pathologic anatomy of the lungs in children with special reference to the hilus, the fissures, and the bronchial distribution.

The author points out, that while there is nothing really specific in the roentgen images of the thorax in the diseases under consideration, there are certain characteristics which may 'suggest' their presence. The main interest of the book lies in the review of all possible thoracic findings in children suffering from the diseases mentioned, the comparison of the roentgen images, and the effort to group these alterations, if not into a specific picture, at least to use the author's own words, into something that 'looks familiar'.

LA TOMOGRAFIA NELLE MALATTIE DEI SENI PARANASALI. CONTRIBUTO CLINICO RADIOLOGICO. By ENRICO BOZZI, Docente, Primario di Otorinolaringoiatria dell'Ospedale Civile di Monza, and LUDOVICO MUCCI, Docente Dirigente la Sez. Radiol. della Clinica Chirurgica dell'Università di Milano. A volume of 152 pages with 140 illustrations. Licinio Cappelli, Bologna, 1947.

The authors have studied 117 pathological sinuses by means of plain and of laminagraphic roentgenograms and this monograph is an account of their experiences. It is richly illustrated (140 figures), well printed on good paper, and because of the wealth of illustration can be studied with profit by those who are interested in laminagraphy of the sinuses.

The largest amount of space is devoted to case histories, in which the patients are described in minute and perhaps unnecessary detail. These histories are preceded by a short introduction and are followed by the conclusion. The authors confirm the value of laminagraphy and maintain that it finds great usefulness in demonstration of the amount of bony damage suffered by the walls of the sinuses either by osteoporosis following purulent sinusitis or by pressure atrophy in cysts and tumors. The diagnosis of polypoid hypertrophy of the mucosa is also facilitated by the demonstration of cyclic contours in laminagraphic films, while the plain films show only uniform cloudiness.

This monograph has the good points and the pitfalls of many similar European works. It combines excellent pictorial demonstration with excessive and perhaps unimportant details within the text.

In Memoriam

FORREST LeROY SCHUMACHER, M.D.

1885-1947

Forrest LeRoy Schumacher died at his home in Bellevue, Penna., June 2, 1947. He was born in Hazleton, Penna., Dec. 12, 1885, and was graduated from the University of Pennsylvania in 1908. After serving in internship at the Allentown Hospital, he began the practice of medicine in Dubois, Penna. In 1910 he undertook the study of radiology at the Mercy Hospital, Baltimore, Md., and in 1914 was appointed to the staff of the Dubois Hospital.

Dr. Schumacher was one of the organizers and a charter member of the Roentgen Ray Society of Central Pennsylvania, now the Pennsylvania Radiological Society, and was president of the society in 1918-1919. In 1923 he was made associate roentgenologist at St. Francis Hospital, Pittsburgh, and in the same year became associated with Dr. Zoe Allison Johnston in private practice. In 1927 he received the appointment of roentgenologist to the Suburban General Hospital, Bellevue, Penna., and to the Homestead Hospital, Homestead, Penna., and in 1928 became radiologist to the Pittsburgh Skin and Cancer Foundation. In 1935 Dr. Schumacher joined the Radiological Staff of the Falk Clinic of the University of Pittsburgh and was made instructor in the Department of Radiology. In the same year he was certified as a diplomate by the American Board of Radiology. He was a member of the Radiological Society of North America and a fellow of the American College of Radiology. He served as President of the Pittsburgh Roentgen Society in 1937.

Dr. Schumacher was married in October 1917 to Miss Emma Veil, of Punxsutawney, Penna., who survives him. Their son, Forrest V. Schumacher, M.D., is at present serving with the Army of the United States, holding the rank of Captain.

H. NORTON MAWHINNEY, M.D.

RADIOLOGICAL SOCIETIES SECRETARIES AND MEETING DATES

Editor's Note Secretaries of state and local radiological societies are requested to cooperate in keeping this section up to-date by notifying the editor promptly of changes in officers and meeting dates Address Howard P Doub, M D, The Henry Ford Hospital, Detroit 2, Mich

UNITED STATES

RADIOLOGICAL SOCIETY OF NORTH AMERICA *Secretary Treasurer*, Donald S Childs, M D, 607 Medical Arts Bldg, Syracuse 2, N Y

AMERICAN RADIUM SOCIETY *Secretary*, Hugh F Hare, M D, 605 Commonwealth Ave, Boston 15, Mass

AMERICAN ROENTGEN RAY SOCIETY *Secretary*, Harold Dabney Kerr, M D Iowa City, Iowa

AMERICAN COLLEGE OF RADIOLOGY *Secretary*, Mac F Cahal, 20 N Wacker Dr Chicago 6, Ill

SECTION ON RADIOLOGY, A M A *Secretary*, U V Portmann, M D, Cleveland Clinic, Cleveland 6, Ohio

Alabama

ALABAMA RADIOLOGICAL SOCIETY *Secretary Treasurer*, Courtney S Stickley M D, Bell Bldg Montgomery Next meeting at the time and place of the Alabama State Medical Association meeting

Arkansas

ARKANSAS RADIOLOGICAL SOCIETY *Secretary*, Fred Hames M D Pine Bluff Meets every three months and annually at meeting of State Medical Society

California

CALIFORNIA MEDICAL ASSOCIATION SECTION ON RADIOLOGY *Secretary* Sydney F Thomas M D Palo Alto Clinic Palo Alto

LOS ANGELES COUNTY MEDICAL ASSOCIATION RADIOLOGICAL SECTION *Secretary* Morris Horwitz M D 2009 Wilshire Blvd Los Angeles 5 Meets second Wednesday of each month at County Society Bldg

PACIFIC ROENTGEN SOCIETY *Secretary*, L Henry Garland M D 450 Sutter St, San Francisco 8 Meets annually with State Medical Association

SAN DIEGO ROENTGEN SOCIETY *Secretary* R F Niehaus M D 1831 Fourth Ave San Diego Meets first Wednesday of each month

X RAY STUDY CLUB OF SAN FRANCISCO *Secretary* Ivan J Miller M D 2000 Van Ness Ave Meets monthly on the third Thursday at 7 45 P M January to June at Lane Hall Stanford University Hospital and July to December at Toland Hall University of California Hospital

Colorado

DENVER RADIOLOGICAL CLUB *Secretary* Mark S Donovan M D 306 Majestic Bldg Denver 2 Meets third Friday of each month at the Colorado School of Medicine and Hospital

Connecticut

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY *Secretary*, Robert M Lowman, M D, Grace-New Haven Hospital, Grace Unit, New Haven Meetings bimonthly, second Thursday

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FLORIDA RADIOLOGICAL SOCIETY *Secretary Treasurer* J A Beals, M D, St Luke's Hospital, Jacksonville Meets semiannually, in April, preceding the annual meeting of the Florida Medical Society, and in November

Georgia

GEORGIA RADIOLOGICAL SOCIETY *Secretary Treasurer*, Robert Drane, M D, De Renne Apartments, Savannah Meets in November and at the annual meeting of State Medical Association

Illinois

CHICAGO ROENTGEN SOCIETY *Secretary*, T J Wachowski M D 310 Ellis Ave, Wheaton Meets at the Palmer House, second Thursday of October, November, January, February, March and April, at 8 00 P M

ILLINOIS RADIOLOGICAL SOCIETY *Secretary-Treasurer*, William DeHollander M D St Johns' Hospital, Springfield Meetings quarterly as announced

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY *Secretary* Frank S Hussey, M D, 250 East Superior St, Chicago 11

Indiana

INDIANA ROENTGEN SOCIETY *Secretary-Treasurer*, J A Campbell, M D, Indiana University Hospitals Indianapolis 7 Annual meeting in May

Iowa

IOWA X-RAY CLUB *Secretary* Arthur W Erskine, M D 326 Higley Building Cedar Rapids Meets during annual session of State Medical Society

Kentucky

KENTUCKY RADIOLOGICAL SOCIETY *Secretary-Treasurer* Sydney E Johnson M D, 101 W Chestnut St Louisville

LOUISVILLE RADIOLOGICAL SOCIETY *Secretary Treasurer* Everett L Pirkey Louisville General Hospital Louisville 2 Meets second Friday of each month at Louisville General Hospital

Louisiana

LOUISIANA RADIOLOGICAL SOCIETY *Secretary Treasurer* Johnson R Anderson M D No Louisiana Sanitarium Shreveport Meets with State Medical Society

ORLEANS PARISH RADIOLOGICAL SOCIETY *Secretary*, Joseph V Schlosser, M D, Charity Hospital of Louisiana, New Orleans 13 Meets first Tuesday of each month

SHEPHERD RADIOLOGICAL CLUB *Secretary* Oscar O Jones M D, 2022 Greenwood Road Meets monthly September to May, third Wednesday, 7 30 P M

Maryland

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Michigan

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MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS *Secretary, Treasurer* R B MacDuff M D, 220 Genesee Bank Building Flint 3

Minnesota

MINNESOTA RADIOLOGICAL SOCIETY *Secretary*, C A Borman, M D, 802 Medical Arts Bldg Minneapolis 2 Regular meetings in the Spring and Fall

Missouri

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY *Secretary* John W Walker, M D, 306 E 12th St, Kansas City, Mo Meetings last Friday of each month

ST LOUIS SOCIETY OF RADIOLOGISTS *Secretary* Edwin C Ernst, M D 100 Beaumont Medical Bldg Meets on fourth Wednesday of each month, October to May

Nebraska

NEBRASKA RADIOLOGICAL SOCIETY *Secretary-Treasurer* O A Neely, M D, 924 Sharp Building, Lincoln Meetings third Wednesday of each month at 6 P M in either Omaha or Lincoln

New England

NEW ENGLAND ROENTGEN RAY SOCIETY *Secretary Treasurer*, George Levene M D Massachusetts Memorial Hospitals, Boston Mass Meets monthly on third Friday at Boston Medical Library

New Hampshire

NEW HAMPSHIRE ROENTGEN SOCIETY *Secretary-Treasurer*, Albert C Johnston, M D, Elliot Community Hospital Keene Meetings quarterly in Concord

New Jersey

RADIOLOGICAL SOCIETY OF NEW JERSEY *Secretary* Raphael Pomerantz M D 31 Lincoln Park New-

ark 2 Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called

New York

ASSOCIATED RADIOLOGISTS OF NEW YORK, Inc. *Secretary* William J Francis, M D, East Rockaway L I

BROOKLYN ROENTGEN RAY SOCIETY *Secretary Treasurer*, Abraham H Levy, M D, 1354 Carroll St, Bklyn 13 Meets fourth Tuesday of every month, October to April

BUFFALO RADIOLOGICAL SOCIETY *Secretary Treasurer* Mario C Gian, M D, 610 Niagara St, Buffalo 1 Meetings second Monday evening each month, October to May, inclusive

CENTRAL NEW YORK ROENTGEN SOCIETY *Secretary-Treasurer*, Dwight V Needham, M D, 608 E Genesee St, Syracuse 10 Meetings in January, May, and October

LONG ISLAND RADIOLOGICAL SOCIETY *Secretary*, Marcus Wiener M D 1430 48th St, Brooklyn 19 Meetings fourth Thursday evening each month at Kings County Medical Bldg

NEW YORK ROENTGEN SOCIETY *Secretary* Wm Snow M D, 941 Park Ave New York 28

ROCHESTER ROENTGEN RAY SOCIETY *Secretary*, Murray P George, M D, 260 Crittenden Blvd, Rochester 7 Meets at Strong Memorial Hospital, third Monday September through May

North Carolina

RADIOLOGICAL SOCIETY OF NORTH CAROLINA *Secretary Treasurer*, James C Hemphill M D, Professional Bldg, Charlotte 2 Meets in May and October

North Dakota

NORTH DAKOTA RADIOLOGICAL SOCIETY *Secretary* Charles Heilman M D, 1338 Second St, N Fargo

Ohio

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CENTRAL OHIO RADIOLOGICAL SOCIETY *Secretary*, Edward T Kirkendall M D 700 North Park St, Columbus 8

CINCINNATI RADIOLOGICAL SOCIETY *Secretary*, Eugene L Saenger M D 735 Doctors Bldg Cincinnati 2 Meets last Monday of the month September to May

CLEVELAND RADIOLOGICAL SOCIETY *Secretary-Treasurer*, George L Sackett M D 10515 Carnegie Ave Cleveland 6 Meetings at 6 30 P M on fourth Monday October to April inclusive

Oklahoma

OKLAHOMA STATE RADIOLOGICAL SOCIETY *Secretary-Treasurer* Peter M Russo M D 230 Osler Building Oklahoma City Meetings three times a year

Oregon

OREGON RADIOLOGICAL SOCIETY *Secretary Treasurer*, Wm Y Burton, M D, 242 Medical Arts Bldg, Portland 5 Meets monthly, on the second Wednesday, at 8 00 P M, in the library of the University of Oregon Medical School

Pacific Northwest

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY *Secretary Treasurer*, Sydney J Hawley, M D, 1320 Madison St, Seattle 4, Wash Meets annually in May

Pennsylvania

PENNSYLVANIA RADIOLOGICAL SOCIETY *Secretary-Treasurer*, James M Converse M D, 416 Pine St, Williamsport 8 Meets annually

PHILADELPHIA ROENTGEN RAY SOCIETY *Secretary*, Calvin L Stewart, M D Jefferson Hospital, Philadelphia 7 Meets first Thursday of each month at 8 00 P M from October to May in Thomson Hall, College of Physicians, 21 S 22d St

PITTSBURGH ROENTGEN SOCIETY *Secretary-Treasurer*, R P Meader, M D 4002 Jenkins Arcade, Pittsburgh 22 Meets second Wednesday of each month at 6 30 P M October to June

Rocky Mountain States

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY *Secretary-Treasurer* Maurice D Frazer, M D Lincoln Clinic, Lincoln Nebr

South Carolina

SOUTH CAROLINA X RAY SOCIETY *Secretary Treasurer*, Robert B Taft M D 103 Rutledge Ave, Charleston 16

Tennessee

MEMPHIS ROENTGEN CLUB Meetings second Tuesday of each month at University Center

TENNESSEE RADIOLOGICAL SOCIETY *Secretary Treasurer*, J Marsh Frère, M D, 707 Walnut St, Chattanooga Meets annually with State Medical Society in April

Texas

DALLAS FORT WORTH ROENTGEN STUDY CLUB *Secretary* X R Hyde, M D, Medical Arts Bldg, Fort Worth 2 Meetings on third Monday of each month in Dallas in the odd months and in Fort Worth in the even months

TEXAS RADIOLOGICAL SOCIETY *Secretary-Treasurer*, R P O'Bannon M D 650 Fifth Ave Fort Worth 4 Next meeting Jan 17, 1948

Utah

UTAH STATE RADIOLOGICAL SOCIETY *Secretary Treasurer* M Lowry Allen, M D, Judge Bldg, Salt Lake City 1 Meets third Wednesday, January, March, May, September, November

UNIVERSITY OF UTAH RADIOLOGICAL CONFERENCE *Secretary*, Henry H Lerner, M D Meets first and third Thursdays, September to June, inclusive, at Salt Lake County General Hospital

Virginia

VIROINIA RADIOLOGICAL SOCIETY *Secretary*, E Latan Flanagan, M D, 215 Medical Arts Bldg, Richmond 19

Washington

WASHINGTON STATE RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Homer V Hartzell M D 310 Stimson Bldg, Seattle 1 Meetings fourth Monday October through May at College Club Seattle

Wisconsin

MILWAUKEE ROENTGEN RAY SOCIETY *Secretary-Treasurer* C A H Fortier, M D, 231 W Wisconsin Ave Milwaukee 3 Meets monthly on second Monday at the University Club

RADIOLOGICAL SECTION OF THE WISCONSIN STATE MEDICAL SOCIETY *Secretary*, S R Beatty, M D, 185 Hazel St, Oshkosh Two day meeting in May and one day at annual meeting of State Medical Society in September

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE Meets first and third Thursdays 4 to 5 P M, September to May inclusive, Room 301, Service Memorial Institute, 428 N Charter St Madison 6

CANADA

CANADIAN ASSOCIATION OF RADIOLOGISTS *Honorary Secretary Treasurer*, E M Crawford, M D, 2100 Marlowe Ave, Montreal 28, Quebec Meetings in January and June

LA SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES *General Secretary*, Origène Dufresne, M D, Institut du Radium, Montreal Meets on third Saturday of each month

CUBA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA Offices in Hospital Mercedes Havana Meets monthly

MEXICO

SOCIEDAD MEXICANA DE RADIOLOGÍA Y FISIOTERAPIA *General Secretary*, Dr Dionisio Pérez Cosío, Marsella 11, México, D F Meetings first Monday of each month

ORLEANS PARISH RADIOLOGICAL SOCIETY *Secretary*, Joseph V Schlosser, M D, Charity Hospital of Louisiana New Orleans 13 Meets first Tuesday of each month

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cranial nerves and the nasopharynx, explaining the cranial nerve signs encountered

Roentgen therapy in this series of cases showed a single cure of more than five years duration, in a lymphoepithelioma. Several patients had been treated recently and the remainder had recurrences or had died of cancer

Illustrative cases are presented

SYDNEY F THOMAS, M D

Odontogenic Tumors A Survey of 75 Cases Kurt H Thoma and Henry M Goldman *Am J Orthodontics* 32 763-790, December 1946

A new classification of odontogenic tumors is presented together with a description of each type. The authors also discuss the inductive effects of one tissue upon another as in the mixed types—those containing fibrous connective tissue and dentine with epithelial strands. They suggest an analogy to the situation in the early embryo, where differentiation of a tissue such as muscle leads to the differentiation of a fascia surrounding it. A number of good roentgenograms and photomicrographs are reproduced. The classification is as follows

- I Epithelial tumors
 - 1 Adamantoblastoma
 - 2 Enameloma
- II Mesenchymal tumors
 - 1 Odontogenic fibroma
 - 2 Dentinoma
 - 3 Cementoma
- III Odontogenic mixed tumors (or odontomas)
 - 1 Soft odontoma
 - 2 Soft and calcified odontoma (adamantoblastoma arising in conjunction with an odontoma but not as well differentiated as the completely formed odontoma)
 - 3 Completely formed odontoma with enamel, dentine pulp, cementum, periodontal membrane
 - (a) Compound (many small teeth)
 - (b) Complex (irregular tooth structure)

This is an excellent paper, but of such length and so rich in detail that an entirely adequate abstract cannot be made

ZAC. F. ENDRESS M D

THE CHEST

Tuberculosis in Industry Frederick Heaf *Brit M J* 2 975-979 Dec 28 1946

Heaf points out that not only is the age when the primary tuberculous infection is received rising but that the age group showing the highest incidence of tuberculosis is also higher. The rate of discovery of cases has increased so that the rise in incidence does not represent a true increase in development of the disease. Some consider that the increase in case finding mainly by radiography accounts for 50 per cent of the rise. Poor hygienic conditions are probably the chief factors in the remaining 50 per cent since where resistance is maintained at a high level as in sanatoria or village settlements constant contact with highly infectious cases fails to produce tuberculosis in the large majority of the staff.

While harmless dusts may indirectly spread tuberculosis by causing chronic catarrh in individuals with undiscovered active lesions, other dusts bear a specific relationship to the development of the disease. Among the grinders of Sheffield the death rate from respiratory tuberculosis in 1938 was reported to be four times the rate for all persons over fifteen in Sheffield. Of 1,397 deaths due to silicosis in 1932-39, active tuberculosis was present in 797 cases. Numerous reports have shown that dormant tuberculous lesions may become active when a simple silicosis has developed. Light work under bad conditions can be more harmful than heavy work under good conditions, and heavy work and poor economic conditions are a serious combination.

In conclusion, Heaf states that occupations rarely cause tuberculosis, but conditions of labor can predispose to it. A fundamental principle is the exclusion of infectious persons (in part by mass radiography) from normal industry. However, pre employment radiography imposes a liability on the employer when engaging proved healthy persons in a hazardous industry.

ELLWOOD W GODFREY M D

Tuberculosis in the Alabama State Hospitals Mass Radiography for Its Control A H Russakoff *Am Rev Tuberc* 55 93-101, January 1947

The author reports the results of a mass survey of the chests of patients confined to several of the Alabama State Hospitals for mental patients. Thirty five millimeter film was used and all suspects were checked with 14 X 17-inch films. The material is presented in tabular form. A total of 3,272 white and 1,865 colored patients were examined. The prevalence of tuberculosis was found to be 5.4 per cent for the white and 2.3 per cent for the colored patients. The incidence was highest for the white males (6.6 per cent) and lowest among the colored males (2.1 per cent).

L W PAUL, M D

The Azygos Lobe in Photofluorography Walter O Pendley *U S Naval M Bull* 46 1920-1927, December 1946

The azygos lobe was discovered by the anatomists as early as 1778 but the first description of its appearance on the roentgenogram was that of Wessler and Jaches in 1923 (*Clinical Roentgenology of Diseases of the Chest*, Troy, N Y, Southworth Co., 1923). It is now generally agreed that the azygos lobe is not congenital in origin but is a developmental phenomenon. Three types have been described: type A, more or less horizontal, cutting the outer or lateral border of the lung at some point between the apex and a position 2 inches below; type B, more nearly vertical, dividing the apex into lateral halves; type C, vertical, cutting off a small tongue-shaped lobe from the inner or mediastinal surface, the pedicle being attached to the upper margin of the lung root.

In a study of 25,000 fluororoentgenograms, the author found 404 instances of azygos lobe, an incidence of 1.6 per cent. Type A constituted 3.71 per cent of the group (15 cases), Type B 81.19 per cent (328 cases), and Type C 15.1 per cent (61 cases).

The chief significance of the azygos lobe in photofluorographic studies is the confusion which it may cause and its possible misinterpretation as disease of the lung. It may itself be the seat of disease; there are reports in the literature of complete atelectasis of the

ROENTGEN DIAGNOSIS

Radiology and the General Practitioner Bede J Harrison Canad M A J 55 576-580, December 1946

The percentage of radiological amateurs in the medical profession is quite high. Many seem to think that any x ray film has its full story plainly written in the photographic emulsion for anyone to read who wishes. With practically no understanding of the principles of technique, and in complete ignorance of the laws of perspective, projection and penetration the amateur radiologist will proceed to infer the presence or absence of a pathological condition on the basis of films for the production and explanation of which he lacks the necessary basic knowledge.

It is the author's feeling that medical students are not being taught radiology properly. We must dismiss the idea that a student should be taught to recognize a disease from the film. We must remember that he is being trained as a general practitioner and that what will help him most is the knowledge of what lesions and what diseases can produce radiological changes. Instead of working from the film back to the disease, the student must be taught to look in the other direction and to proceed from the differential diagnosis to the x ray investigation. BERT H. MALO, M.D.

Roentgenologic Diagnosis Changes Resulting from Chemotherapy Arthur C Christie and George M Wyatt J A M A 132 895-898 Dec 14, 1946

The use of penicillin, the sulfonamide compounds and allied products has so greatly altered the course of many infectious diseases that revision of roentgenologic criteria for diagnosis is necessary. Several cases are cited illustrating the changes in pathologic anatomy resulting from the use of these drugs.

A boy of four had swelling, redness, and extreme tenderness of the wrist four days after eruption of pustular chicken pox. A total of 1,510,000 units of penicillin was given parenterally in eleven days. The symptoms promptly subsided. Roentgenograms two days after onset showed no bony abnormality. Two days later a small area of bone destruction at the distal end of the radius was visualized and a definite diagnosis of osteomyelitis was made. Films eleven months later showed only a slight scar at the site of the original disease and no disturbance in bone growth. The complete series of films with the history and record of treatment made an understandable picture, while a single film might have been very confusing. Adequate dosage of penicillin killed the organisms of osteomyelitis *in situ* and entirely altered the course of the disease.

Four cases are presented to illustrate the partial attenuation of infection by inadequate therapy, converting an acute infection into a chronic one of low-grade virulence with resultant roentgenographic changes. It will suffice to summarize one of these here. A woman, twenty-four, had severe pain in the right thigh two weeks after a tonsil infection(?). She had clinical and laboratory evidence of infection, though the roentgenogram showed no abnormality. She was given 18 gm of sulfadiazine in forty-eight hours. Three months later roentgen study showed extensive moth-eaten destruction of the entire femoral shaft with elevated periosteum and subperiosteal new bone. She was given 1,000,000 units of penicillin parenterally in eight days. Two months later a roentgenogram showed com-

plete healing of osteomyelitis with decided thickening of the femoral cortex.

Still another case illustrates the effect of inadequate penicillin therapy on a soft tissue abscess: the presence of which was unsuspected. A man, twenty-three, had a hard, fixed mass in the right upper quadrant of the abdomen with intermittent pain in the right side for two years. Prior to this he had had carbuncles which cleared spontaneously and a gonorrheal infection treated with 200,000 units of penicillin. A roentgenogram made during this time showed enlargement of the upper pole of the right kidney and pressure deformity of the upper calyx. Later pyelographic studies suggested renal tumor, but a final diagnosis of perinephric abscess was made. Surgical exploration confirmed this diagnosis.

The authors emphasize the necessity of careful analysis of the history and therapeutic management of infectious diseases if accurate diagnosis and prognosis are to be made from roentgenologic studies, particularly when inadequate therapy has been used.

BERNARD S. KALAYJIAN, M.D.

THE HEAD AND NECK

Intracranial Air Studies in Infants and Children. Martin Schneider. Texas State J Med 42 480-489 December 1946

Six pediatric cases are presented in which the clinical history and neurological examination suggested diagnoses which were confirmed or modified by intracranial pneumography. The author warns of the dangers involved and cites the precautions necessary when the procedure is considered. In his experience the examination has resulted in a reduction of the number of simple decompressions performed. As a result more specific operations and radiotherapy can be carried out. Roentgenograms of representative cases are reproduced including porencephaly, glioblastoma, cyst of the septum pellucidum, cerebellar tumor, medulloblastoma, and a vascular glioma. Brief case reports are also included. In children intracranial air studies are of particular value because so often the histories and even the examinations are unsatisfactory for accurate localization of the lesion. STANLEY H. MACHT, M.D.

Malignant Tumors of the Nasopharynx. A Diagnostic Blind Spot. Radiation Therapy Conference. Simeon T. Cantor and Franz Buschke, Editors. West J Surg 54 404-406 December 1946

There have been accepted for treatment in the Tumor Institute of the Swedish Hospital, Seattle, Wash., since 1939, 18 patients with malignant tumors of the nasopharynx. In 14 of the series the disease was already advanced owing to failure of the physicians previously consulted to recognize the nature of the lesion. In one case even though cervical lymph node involvement was present no attempt was made to discover a primary tumor and a year elapsed before the patient was referred to the Tumor Institute.

An illustration of the base of the skull from the book by Cutler and Buschke (Cancer Diagnosis and Management Philadelphia W. B. Saunders Co. 1938) is reproduced showing the intimate relation between the

The prognosis in the uncomplicated case is excellent, and recovery complete. Active pulmonary tuberculosis develops in these patients no more frequently than in any other similar age group.

CLARENCE E. WEAVER, M D

Resectable Pulmonary Lesions Wm Ray Rumel Rocky Mountain M J 43 989-1002 December 1946

The author begins with a brief statement as to the improved surgical treatment of pulmonary lesions and points to an operative mortality (figures from several clinics being included) of only 1 to 3.5 per cent including lobectomies and pneumonectomies. Most of us who have been in contact with the work of clinics where the advances in pulmonary surgery have been made available will share his enthusiasm and rejoice in the successful attack on one more group of entities which in our student days were passed glumly by as hopeless.

The subject is taken up systematically, beginning with diagnosis, including history and physical examination, laboratory studies, roentgenography and fluoroscopy, bronchography, bronchoscopy, artificial pneumothorax, thoracoscopy, and finally exploratory thoracotomy. The author states at the outset that a differential diagnosis by means of x-rays is usually not possible, along with this he condemns the policy of "watchful waiting" for obvious reasons.

The more significant lesions are taken up in order.

Bronchiectasis In plain films ordinary chronic bronchitis produces just about the same sort of pulmonary markings as does bronchiectasis. Other signs such as mottling or emphysema may be present but less frequently. The bronchogram is diagnostic.

Primary Tumors About 93 per cent of primary pulmonary tumors are malignant. If bronchial adenomas, which often show malignant change, are included, the proportion rises to about 99 per cent. When cough continues over an inordinate interval without obvious etiology, or when the cough is productive of even a small amount of blood-tinged sputum, bronchoscopy is in order. It should be done also in any patient with a unilateral wheeze. Most of the shadows cast by the peripherally located lesions, those outside the stem bronchus, are due to atelectasis. Recurrent attacks of "flu" may signify a pulmonary neoplasm. On the other hand the ordinary appearances of continued health may be maintained.

One case with an obvious moral is cited: the clinical course before operation was long enough that the patient received a good bit of x-ray therapy, four weeks after operation the bronchus opened, producing an empyema which was drained, but the outcome was fatal. [In pulmonary surgery, as in thyroid surgery, one of the obstacles to success would seem to be the ill advised use of radiation while operation is delayed. No one has yet found a satisfactory answer to the question as to how one may expect to control the spread before operation if it cannot be controlled afterwards.—P J D.]

Pulmonary sarcoma is something of a rarity, though the author's series contains 2 cases with survivals of two and three years, respectively.

Bronchial adenomas have been a matter of some dispute: some have considered them thoroughly benign, and dealt with them by bronchoscopy, others consider them potentially malignant and regard thoracotomy as the preferred approach.

Lung Abscess The author feels that the stage of in-

decision is well past in their clinic so far as lung abscess is concerned: he states that the firmly organized and thick-walled variety may as well be despaired of medically, and should be dealt with promptly by surgery, since it constitutes a very considerable menace to life if allowed to remain active.

Cysts Congenital cysts are true cysts, fluid-containing, and should be removed, since they represent a hazard. They are among the lesions most amenable to surgery.

This article is earnestly recommended to all interested in the subject of chest surgery. The author presents his material logically with assurance, and in such a manner that one recognizes the statement of a mature surgeon who is happily free of bias or coloring or any ulterior motive.

PERCY J. DELANO, M D

Cardiac Aneurysm, with an Account of a Case Followed over an Unusually Long Period G H Robertson New Zealand M J 45 527-534, December 1946

In the case recorded here cardiac enlargement was first noted in 1918 while the patient was on duty in the Army, at which time he was twenty-two years old. He suffered from precordial pain and dyspnea on exertion during the next four years, but was then able to carry on hard work for twelve years. In 1935 he had some dyspnea on exertion but continued in his work. In 1937 evidence of aneurysm of the left ventricle was first demonstrated radiographically. There was a localized bulge projecting forward and to the left just above the apex. There was calcification at its periphery and fluoroscopy showed diminished pulsation as compared with the adjacent ventricular border. Electrocardiographic studies were confirmatory.

In the years which followed the patient worked almost continuously at heavy labor such as farm work and road building, taking short periods off because of dyspnea. In 1946 he was still able to work for a few days at a time but became tired easily and had suffocating tightness of the chest if he walked rapidly.

The author reports that at the last examination in April 1946 the aneurysm had not increased in size, but the calcification had gradually progressed and was then quite extensive. The patient was still alive in September 1946.

The author believes this man had cardiac infarction in 1918 while acting as a "runner" in the service, and that the aneurysm developed at the site of the infarct. This would make the present duration of the aneurysm at least twenty-six years. The longest previous survival reported has been ten years.

BERNARD S. KALAYJIAN, M D

Right-Sided Aorta with Atypical Coarctation Involving Only the Left Subclavian Artery Hypertension Arthur M Master Am Heart J 32 778-785, December 1946

The author gives the history of a young, well-developed asymptomatic healthy midshipman, aged twenty-two in whom was found a right-sided aorta, with a coarctation of the left subclavian artery. Promotion was denied him because of a hypertension. Physical examination revealed a short systolic murmur over the base, a slow pulse ranging from 45 to 60 per minute, pulsations in the left carotid, axillary, brachial, and radial arteries weaker than those on the right side. The blood pressure readings on the right arm were

azygos lobe, tuberculosis affecting this lobe alone and pleural effusions into the meso azygos

SYDNEY F. THOMAS, M.D.

Pneumococcosis in Dockers Dealing with Grain and Seeds. Lasar Danner, R. Hermon and D. J. T. Baghall. *Brit J Radiol* 19 506-511, December 1946

The chests of 55 dock workers unloading grain and seeds were studied. The atmosphere was filled with dust arising from the grain (oats, barley, wheat and maize) and seeds (millet, cotton, date, ripe and palm kernel). Twenty six of the workers were found to have active tuberculosis and 4 quiescent tuberculosis, 11 showed reticulation and fibrosis resembling pneumoconiosis and 14 were normal.

The patients with pneumoconiosis to consideration of whom this paper is limited complained of cough with expectoration, which was sometimes blood streaked and dyspnea. There was considerable variation between the physical signs and the x-ray observations.

An analysis of the dusts revealed appreciable amounts of silica, also fine hairs, starch grains and cellular organic matter. No tubercle bacilli were recovered from the dust.

Although no post-mortem confirmation is reported the authors feel that exposure to dust from grains and seeds can produce fibrosis of the lungs.

SYDNEY J. HAWLEY, M.D.

Association of Pneumonia with Erythema Multiforme Exudativum. Commission on Acute Respiratory Diseases. *Arch Int Med* 78 687-710 December 1946

Six cases of erythema multiforme exudativum with predominant involvement of the mucous membranes of the mouth seen during a three year period at the Regional Station Hospital Fort Bragg, N. C., are described. In 3 of the 6 cases, clinical and roentgen evidence of pulmonary involvement was demonstrated. On the basis of clinical and laboratory findings, it was believed that the pulmonary lesions were due to non-bacterial pneumonia. The pneumonia appeared to be an integral feature of the disease and could not readily be considered a secondary complication.

In many respects the pneumonia in the present series of cases bore a close resemblance to primary atypical pneumonia. The prodromal symptoms, absence of physical signs of consolidation, the radiographic character of the lesion, the minimal degree of respiratory distress, the absence of pleural pain or bloody sputum and the relatively normal leukocyte count were features not unlike those commonly encountered in primary atypical pneumonia. The authors believe that it is probable that pneumonia occurs more often in erythema multiforme exudativum than has been recognized. It is now well accepted that instances of mild primary atypical pneumonia can be recognized only by roentgenograms in a considerable percentage of cases. It appears probable that a similar difficulty attends the diagnosis of the pneumonia associated with erythema multiforme exudativum.

Transitory Pulmonary Infiltrations and Apical Cavitation Associated with Eosinophilia. A. Elkeles and N. R. Butler. *Brit J Radiol* 19 512-517 December 1946

Loeffler's syndrome, characterized by transitory pulmonary infiltrations in any part of the lung with eosinophilia, is frequently discovered in mass surveys.

One such case is reported in detail with serial roentgenograms covering a period of six months. This case showed a shadow which indicated cavitation in the apex of one lung, indistinguishable except for its rapid disappearance and the absence of tubercle bacilli, from a tuberculous cavity.

The diagnosis is established by the absence of tubercle bacilli, the rapid disappearance of the infiltrations, the migration of the infiltrations to other parts of the lungs, the eosinophilia, and the disproportion between the clinical symptoms and the extent of pulmonary involvement.

The condition is quite definitely established as allergic in origin. A great variety of allergens may be responsible. Numerous other manifestations of allergy are present in these patients.

SYDNEY J. HAWLEY, M.D.

Simple Spontaneous Pneumothorax in Apparently Healthy Individuals. A Report of Twenty-four Cases. R. F. Nicholas. *Am J Roentgenol* 57 12-27, January 1947

Simple (benign, idiopathic or temporary) spontaneous pneumothorax may be defined as pneumothorax occurring suddenly in otherwise healthy subjects. There is little or no fever and pleural effusion is infrequent or small in amount. Re-expansion of the lung takes place in two to six weeks. Usually there are no residual ill effects. Neither lung shows evidence of active pulmonary tuberculosis. Of the 24 cases reported in this paper 20 were in males and 21 occurred between the ages of twenty and forty years.

Kjaergaard (*Acta med Scandinav* supp 43 1932) maintains that simple spontaneous pneumothorax is due to rupture of a valve vesicle anywhere on the surface of the lung. These vesicles may be due to scar tissue or may be emphysematous or congenital. All three types are believed to have a valve like structure at their pleural attachment. According to Kjaergaard air can pass from a terminal bronchiole into the vesicle but is prevented from passing out again. The vesicle gradually increases in size and pressure is built up with thinning of the wall of the vesicle. Rupture takes place when pressure is suddenly increased, as in coughing or sneezing. Kjaergaard thinks it impossible for a normal pleura to rupture through coughing or by muscular exertion. Rupture does not occur in bullous emphysema because no valve like mechanism exists and positive pressures are not built up in the blebs.

The clinical picture in simple spontaneous pneumothorax is usually one of sudden onset of pain on the side of the pneumothorax and shortness of breath. A history of physical exertion preceded the onset in the author's series in about 35 per cent. The acute symptoms usually subsided in a few days. The average period of time for complete re-expansion of the collapsed lung was five weeks. Nine of the 24 patients experienced a recurrent pneumothorax. 2 had alternating spontaneous pneumothorax and 7 had collapse of the same lung.

Two patients in this study have been treated for recurrent spontaneous pneumothorax by the induction of a chemical pleuritis and one patient by thoracotomy. All three have remained asymptomatic for periods varying from two to six years. Follow up studies show 20 of the 24 patients to be in good health. Three have not been adequately followed. One has had a coronary occlusion but is alive.

the case is the fact that the clasp of the denture remained impacted in the upper part of the wall of the esophagus for more than five weeks, producing considerable local reaction, which, however, subsided rapidly after removal of the foreign body. It is pointed out that some dentures are made without clasps, and that roentgenography would be of no value in locating these, should they become impacted in the air or food passages.

Gastragogue Effect of Laxatives and Allyl-Bromide-Mixture Henry M Feinblatt and Edgar A Ferguson, Jr. *Am J Digest Dis* 13 386-390, December 1946

The word "gastragogue" has been coined to identify a substance that will hasten the emptying of the stomach. To study the effect of cathartics on gastric emptying 7 patients were given a barium meal and in six hours films were taken in the vertical and horizontal axes. A repeat examination was done in each case with the same mixture of barium followed by a laxative containing aloin, cascara, extract of rhubarb and phenolphthalein. A comparison study of the cases showed that there was very little difference in the amount of retention in the stomach after six hours. A study of various other cathartics showed no effect on stomach emptying time. The effect of allyl bromide was then studied, the same series of patients being given two 5-gram tablets of the allyl bromide mixture with the barium meal two tablets two hours later, and two tablets four hours later. It was found that the patients who had fairly marked retention in the other tests had little or no retention after six hours when the allyl bromide was given. JOSEPH T DANZER, M D

Early Indications of Adhesive Small Bowel Obstruction Claude J Hunt. *Am J Surg* 72 865-868 December 1946

The early diagnosis of small bowel obstruction is dependent upon the correlation of three characteristic clinical findings with proper interpretation of radiographic findings. The clinical findings are synchronous typical, diffuse, colicky abdominal pain, visible peristaltic waves, and metallic borborygmi. The second finding, visible peristalsis, may be absent if the degree of distention is great. In addition the presence of a protruding mass on the surface of the abdomen is considered evidence of strangulation. Vomiting and the passage of gas and feces are not reliable signs, as they may or may not occur. The degree of abdominal tenderness and rigidity is said to be less than that seen in specific colics or acute localized inflammation.

The x ray examination is the only positive means of establishing early diagnosis with differentiation between strangulated and non strangulated obstruction. The characteristic roentgen findings of gas in the small bowel, the typical 'stairstep' pattern and visualization of the valvulae conniventes are described as diagnostic of non strangulated obstruction of the small bowel. A strangulated obstruction is described as having no definite pattern but the valvulae conniventes are not visualized due to the extravasation of blood into the lumen of the bowel, and the distended loops arrange themselves in whatever portion of the abdomen the obstruction occurs. Proximal distention is slow to appear in this type of obstruction.

Decision as to the type of treatment requires an accurate diagnosis. Non strangulated obstruction does

not demand immediate operation, and the patient may be prepared by chemical and fluid rehabilitation and bowel decompression. Strangulated obstruction, however, requires immediate surgery.

The author emphasizes the importance of competent assistance by the radiologist in establishing the diagnosis and thereby determining the choice of treatment.

PAUL R. NOBLE, M D

Present Status of the Problems of Regional Ileitis John H Garlock. *Am J Surg* 72 875-878, December 1946

An experience of approximately 200 instances of regional ileitis has led the author to recognize five symptomatic groups. (1) In *acute ileitis* the history and findings so closely resemble appendicitis that only rarely can a preoperative diagnosis be made. (2) *Chronic enteritis* usually presents the triad of foul, non-bloody diarrhea and cramps, loss of weight, and anemia. Abscesses and fistulae are common complications. (3) A third group is that showing *obstructive symptoms* due to diminution of the caliber of the small bowel. (4) In some cases symptoms may be due to involvement of adjacent viscera—the bladder, rectum, cecum, or pelvic organs. (5) In the fifth group the significant feature is the presence of external fecal fistulae. The author states that in his experience the most common cause for fecal fistula following appendectomy is an underlying ileitis. The pathogenesis is not believed to be a 'blowing out' of the stump, but perforation of an ileal ulcer into the mesentery and fixation to the abdominal wall followed by operative or spontaneous rupture, usually in the right lower quadrant.

X-ray examination should include a barium enema study, which will serve to rule out a concomitant ulcerative colitis and may demonstrate the narrowed ileum if the ileocecal valve is incompetent. Regardless of findings in such a study, a gastro intestinal series should be done to demonstrate the presence or absence of disease in the upper ileum or jejunum.

The treatment of ileitis is surgical except in those patients with a short history of diarrhea, suggestive x-ray findings and no weight loss or disabling symptoms. The majority of these latter patients remain relatively well and show no change roentgenographically on follow-up examination. In the event that ileitis is found during an operation for acute appendicitis, nothing further should be done.

The operation recommended is ileocolostomy with exclusion, statistics showing better results with this procedure than with more extensive surgery. A number of practical points in the management of ileitis are given.

PAUL R. NOBLE, M D

Motor Dysfunction of the Biliary Tract. An Analytical and Critical Consideration A C Ivy. *Am J Roentgenol* 57 1-11 January 1947

The gallbladder is evacuated by way of the cystic duct under the force of contraction which is caused primarily by the action of the hormone cholecystokinin. This hormone is produced by the upper intestinal mucosa when in contact with acid, fat, or partially digested protein. It is not produced in response to a carbohydrate meal or water. In all animals that have a gallbladder the common duct possesses a sphincteric mechanism which is intimately co-ordinated with duodenal tone and motility but which may also act independently. It is possible for a spastic sphincter to exert

158-170/60-76, those on the left were 101-124/70-80. The EKG revealed a sinus bradycardia 42 beats per minute. Correlation was suspected because of the hypertension in the right upper extremity, but the diagnosis was dismissed for lack of other corroborating evidence. X-ray studies revealed a right-sided aorta. The esophagus, at the level of the aortic arch, was found to be displaced anteriorly and to the left of the aorta. There were no cervical ribs. A congenital anomaly of the left subclavian was suspected to account for the small pulse. An angiocardioradiographic examination disclosed an enlargement of the left ventricle, displacement of the interventricular septum to the right, and an stenosis of the left subclavian artery. There was no narrowing of the aorta.

The author believes that a localized coarctation of the left subclavian artery should be considered in a patient with a small or absent left radial pulse, a hypertension in the right arm, and normal expected blood pressure in the femoral vessels after the exclusion of a large cervical rib, an anatomic variation of the radial artery, an aortic aneurysm, and tumor compressing the left subclavian artery. HENRY K. TAYLOR, M.D.

Pentoneopericardial Diaphragmatic Hernia. Report of a Case in a Newborn Infant Successfully Corrected by Surgical Operation with Recovery of the Patient. Angus K. Wilson, William R. Rummel, and O. I. Ross. *Am J Roentgenol* 57:12-19, January 1947.

Only 5 cases of pentoneopericardial diaphragmatic hernia were discovered by the authors in a careful search of the literature. In 2 of these operation was done, but the patients failed to survive. Five cases disclosed at autopsy were without symptoms, hence it would appear that the defect is not imminent to life. An accurate diagnosis has not been made prior to operation or autopsy examination.

The authors report a case with herniation of the abdominal contents into the pericardium. The patient survived operation, which was performed at the age of seven weeks, and was still without symptoms seven months later when this report was made. Clinically the condition cannot be distinguished from the more common pentoneopericardial diaphragmatic herniae. Pentoneopericardial herniation should be suspected in all cases showing cardiorespiratory embarrassment especially those having postprandial cyanosis relieved by vomiting. The diagnosis can be made roentgenologically if coils of intestine can be identified by gas or opaque medium content obscuring the cardiac shadow and within the confines of the distended pericardium.

CLARENCE E. WEAVER, M.D.

THE DIGESTIVE SYSTEM

A Contribution to the Roentgen Diagnostics of Limited Esophagitis. Solvej Wehn. *Acta radiol* 27:401-471, May 6, 1946.

While inflammatory changes in the esophagus particularly in the lower third, are quite common in post mortem material the diagnosis is not commonly made antemortem. The author reviews the literature and presents 9 cases in which the diagnosis was made clinically and confirmed microscopically. The predominant symptom in all cases was progressive dysphagia. In 5 of the cases an original diagnosis of cancer had been made.

The typical course of esophagitis may be divided into three stages. In early cases the mucous membrane is edematous and bleeds easily, roentgenologically the thick folds and stiffness of the wall are suggestive but the differentiation from carcinoma is difficult. In the second stage the mucous membrane of the upper portion is relatively normal while that in the lower portion is inflamed and covered by fibrin. The roentgenologic picture is that of an elongated smooth funnel-shaped constriction of the lower portion. In the final stage the mucous membrane is thin, pale, and scarred and on fluoroscopic or roentgen examination the constriction is smooth with a sharply demarcated upper margin but usually indistinct lower end, and there is more or less dilatation above. Several illustrations are included.

ELIZABETH A. CLARK, M.D.

Simple Non-Sphincteric Localized Esophageal Spasm. Case Report. Morris Weiss and Leonard Long. *Am J Digest Dis* 13:375-377, December 1946.

The more common spasms of the esophagus are of two types: (1) sphincteric (cricopharyngeal spasm and cardiospasm) and (2) non-sphincteric secondary to organic disease. Simple non-sphincteric spasm, because of its mild symptoms is not often diagnosed. It may occur in any age group and both sexes are equally affected. The cause of this condition is not clear but nervous instability is usually a predominating factor. The outstanding symptoms are dysphagia and substernal pain which may vary from a dull ache to severe piroxyms resembling angina pectoris.

A case report is given of a colored soldier who was admitted to the hospital complaining of inability to swallow and substernal pain. He gave an indefinite history of having swallowed lice at the age of five and of having intermittent attacks of dysphagia at irregular intervals thereafter. The last attack occurred about a year before at another army camp. Barium paste was swallowed with some difficulty stopping abruptly at the level of the second thoracic vertebra. No barium passed beyond this point during a fifteen minute period of observation. The patient was given a liquid diet and 1/150 gr of atropine every eight hours. Within twenty-four hours he was able to swallow normally and a second roentgenoscopic study showed no evidence of obstruction. Esophagoscopy examination revealed an area of narrowing beyond which the tube could not be passed without force but when this was repeated after intense sedation the esophagoscope was passed along the entire length of the esophagus. No lesion could be seen. The patient left the hospital in a few days. About two months later he returned with the same symptoms which again disappeared after a week of treatment. JOSEPH T. DANZER, M.D.

A Foreign Body Impacted at the Upper Opening of the Esophagus for Over Five Weeks. Clifford L. Roschfield. *M J Australia* 2:843-844, Dec 14, 1946.

A soldier complained of a sore throat and dysphagia. Roentgenograms revealed two apparently separate wire-like bodies at the level of the hyoid bone and cricoid cartilage respectively. Actually these were attached to an acrylic denture containing five teeth but since this was radiotranslucent it was not demonstrable and was discovered by laryngoscopy only after it was learned that a denture had been missing since an epileptiform attack several weeks earlier. An interesting feature of

tiation from gallstones or renal calculi can be accomplished by contrast visualization, and from lymph node calcification by localization with reference to the duodenal loop. Calcification in vessels or in an aneurysm of the splenic artery may cause confusion, as may also a calcification of the nucleus pulposus or of a cyst wall.

Pancreatic cysts are usually recognized by the pressure defect on the stomach. Carcinoma of the pancreas is often in the tail where it widens the duodenal loop and later compresses the duodenum or stomach. In pancreatitis the swelling may produce this same sign, abnormalities of movement such as reverse peristalsis will mark inflammation. Frostberg has described the 'reversed 3' sign in chronic pancreatitis. Indurative processes, by altering the retrogastric tissues, may produce a horizontal course of the lesser curvature, often with a wavy contour, this may occur in necrotic pancreatitis, infarction or in a thickened, edematous pancreas.

Duodenal diverticula may play a role in pancreatitis, in the literature 50 per cent of patients with duodenal diverticula showed pancreatitis as well. Another sign not infrequently seen in pancreatitis is diminished mobility of the left leaf of the diaphragm, sometimes accompanied by horizontal striations in the left base due to the lessened aeration—plate like atelectasis."

LEWIS G. JACOBS, M D

Pancreatitis as a Cause of Complete Obstruction of the Common Duct. J Dewey Bisgard. *Ann Surg* 124 1009-1018, December 1946

Bisgard reports two cases of obstructive jaundice in which an existing pancreatitis as judged by operative findings and blood amylase studies, was the only demonstrable cause of obstruction of the common duct. In both cases the common and hepatic ducts were dilated while the gallbladder was much smaller than normal contracted, thick walled and without stones. Both patients recovered following prolonged drainage of the common duct.

Cholangiographic studies in both cases ten and eleven days after operation showed absence of filling of the distal intrapancreatic portion of the common duct, with wide dilatation of the duct proximal to this point. The radiopaque solution passed into the duodenum indicating incomplete obstruction.

ELLWOOD W. GODFREY, M D

RETROPERITONEAL TUMORS

Primary Retroperitoneal Tumors. A Report of 95 Cases and a Review of the Literature. Bernard A. Donnelly. *Surg Gynec & Obst* 83 705-717 December 1946

Although primary retroperitoneal tumors are not of common occurrence the author found some 500 cases in the literature to which he adds 95 seen in the University of Iowa Hospitals in the period 1925-45. On the total number of cases the present report is based. Tumors of the retroperitoneal organs are not included.

Retroperitoneal tumors frequently occur in close proximity to the urinary system, gastro-intestinal tract or pelvic brim and present problems of diagnosis to the urologist, gastro-enterologist, general surgeon, and gynecologist. The tumors may arise from the embryologic urogenital cell ridge, adipose tissue, areolar connective tissue, fascia, lymph nodes, lymphatics, or sympathetic nervous structures. They may raise or displace any abdominal viscera and may extend into the mesentery of the sigmoid or colon and the small bowel. They have extended into the pelvic connective tissue. It is thought that they arise from embryonic mesothelial cell rests.

Grossly, primary retroperitoneal tumors may be solid or cystic, or a combination of both. They may be single or multiple. In some bony or calcareous tissue predominates. Though these tumors may be benign they are predominantly malignant. A wide diversity of histologic types is seen. Sarcoma is the most common malignant tumor. Of the benign tumors, lipoma was the most frequently reported in the literature, but epithelial cysts were more common in the author's series. Lipomas frequently undergo sarcomatous change.

Recurrence of retroperitoneal tumors following surgery is common, though whether this is a true recurrence or represents the development of another growth overlooked at operation is not certain. The most frequent sites of metastasis are the lungs, liver, vertebrae, and lymph nodes, in that order.

The symptoms are not pathognomonic but are due to pressure on the gastro-intestinal tract with resultant pain, nausea, loss of weight, loss of appetite and constipation. The pressure may also involve the urinary tract with symptoms of obstruction. The most constant findings are loss of weight and an unexplained abdominal mass.

With adequate examination, the diagnosis of retroperitoneal tumor can be made in a high percentage of cases, although the exact nature of the tumor may not be disclosed. The diagnosis is usually made by exclusion. Retrograde pyelography is considered superior to intravenous pyelography and a very valuable aid in ruling out lesions of the urinary tract. (1) Antero-posterior films will show deflection of the ureter laterally or mesially. (2) lateral films will show anterior displacement of the ureters, (3) the calices will be improperly filled due to pressure from the retroperitoneal tumor, (4) the pelvis of the kidney will be displaced flattened compressed, and rotated by the tumor, (5) muscle shadows may be obliterated, (6) displacement of the bladder may be noted. The chief value of the gastro-intestinal x-ray picture in the diagnosis of retroperitoneal tumors is the excluding of the gastro-intestinal tract as the primary site of the lesion. Quite frequently if the tumor is of sufficient size, the x-ray film shows that the ascending or the descending colon is displaced from its normal position.

The treatment of choice is wide excision of the tumor where it can be done without destroying vital structures. Most of the tumors have been found to be radiosensitive and x-ray therapy is indicated postoperatively, for metastasis and in inoperable cases, and should be given routinely.

VERN W. RITTER, M D

THE MUSCULOSKELETAL SYSTEM

Primary Sarcoma of Bone. Analysis of 71 Cases. Thomas A. Shallow and Frederick B. Wagner, Jr. *Pennsylvania M J* 50 233-239, December 1946

The question of whether or not a bone tumor is malignant is a challenging problem to the clinician,

a resistance to flow greater than the capacity of the gall bladder to contract and greater than the secretory pressure of the liver. This could be a factor in the production of pain. A disturbance in the reciprocal innervation of the gallbladder and the sphincter could delay evacuation of the gallbladder or give rise to increases in intrabiliary tract pressure sufficient to cause symptoms. Morphine and pilocarpine usually cause spasm of the sphincter of Oddi. Magnesium sulfate, amyl nitrate and nitroglycerine cause relaxation.

It seems to have been clearly demonstrated in cholecystectomized patients with a T tube in the common bile duct that spasm of the sphincter of Oddi alone can cause pain. There are also experiments which show that pain may occur from procedures that presumably cause distention of the ducts by physiological pressures in the absence of a T tube or other foreign body.

The difficulty in using evacuation time of the gall bladder (in cholecystography) as a criterion of the normality of the motor activity of the biliary passages is the variability observed. Whether this is due to a difference in the motor activity of the gallbladder or to a difference in the rate of evacuation of the fat from the stomach is unknown. The only solution would seem to be to give a standard stimulus paracaterally. Cholecystokinin would be such a stimulus but this is not at present available for use in man.

Visualization of the hepatic ducts is unusual. It may occur with a normal gallbladder *in situ* with or without pain generally the latter. In the presence of unexplained pain resembling biliary colic in the cholecystectomized patient one must assume the presence of spasm of the sphincter of Oddi and transient physiological obstruction. In some cases the induction of colic with a sixth of a grain of morphine may prove useful.

There is adequate evidence of a physiological nature, provided by a large group of investigators to justify the view that a motor dysfunction of the biliary passages may produce symptoms or that such an entity as biliary dyskinesia exists.

CLARENCE F. WEAVER, M.D.

A Comparison of Two Cholecystographic Media C. A. Stevenson and R. N. Smith, Jr. Texas State J. Med. 42: 492-494 December 1946

A comparative study was made of two media, tetradiodophenolphthalein and priodax, each being used in 500 consecutive gallbladder studies. The tetradiodophenolphthalein was given in 4 gm doses following Kirklin's recommendations in regard to diet, time, preparation and roentgenographic technique (Am J Roentgenol 25: 595 1931). The priodax was given in 3 gm doses as recommended by the manufacturers. The double dose technique was not used. The patients were questioned about nausea, vomiting, diarrhea, burning on urination, abdominal cramps, headache, brackish burning in the throat, bad taste in the mouth, insomnia, and general malaise. The term diarrhea was applied only if there were two or more loose stools.

The authors found that priodax produced 'almost 50 per cent less of all symptoms listed except for burning on urination and burning in the throat. Forty two per cent of all patients receiving priodax complained of burning on urination. There was a higher incidence of symptoms after taking both media than has been reported elsewhere.

So far as the roentgenographic diagnosis is concerned, very little difference was found between the two media. Of the 500 patients receiving tetradiodophenolphthalein, 6 per cent showed the dye in the hepatic flexure. No dye was seen in the colon or small bowel in the group receiving priodax.

Since completing this series, the authors have used priodax in 1,000 cases. They state that the surgical findings have confirmed the roentgenologic diagnosis in a high percentage of all cases. They regard priodax as preferable to tetradiodophenolphthalein because it produces fewer untoward symptoms and is equally good roentgenographically. PAUL W. ROMAN, M.D.

Air in the Biliary Passages: A Review and Report of a Case Dan C. Donald, Burton T. Meadows and S. J. Silbermann. Arch Surg 53: 652-663 December 1946

Although the principal emphasis in the diagnosis of internal biliary fistula has been on the roentgen signs, the authors feel that proper evaluation of the clinical picture will lead to more early diagnoses. Most fistulas are due to infection or calculi. There are extensive adhesions to the bowel and thickening and fibrosis of the gallbladder wall. The clinical picture is similar to that seen in chronic biliary disease, but more severe. Colicky pains, jaundice, chills and fever are the common signs. Diarrhea may be present and occasional patients may be asymptomatic. Roentgen diagnosis is earlier in recent fistulas because of their larger size. The visualization of gas in the bile ducts is due not so much to the size of the fistula as to infection in the biliary tree.

Surgical treatment carries a high mortality, 50 to 60 per cent. This is due to the advanced age of the patients, the initial disease which led to fistula formation, and local changes about the fistula and in the liver. Since many of the cases are not diagnosed preoperatively, preparation of the patient may be inadequate. Moreover, the operation offers more than average technical difficulty because of the local changes in the tissues at the site of the fistula.

In the case reported the presence of the fistula was recognized roentgenographically. A barium fleck, independent of the stream of barium sulfate about the second portion of the duodenum, was interpreted as indicating the site of the fistulous opening between the duodenum and gallbladder and air was seen in the extra-hepatic biliary ducts and biliary radicals. Operation was successful. LEWIS G. JACOBS, M.D.

Pancreatic Disease in the Roentgenogram Max Lüdin. Schweiz med Wchnschr 76: 1273-1274 Dec 14 1946

Roentgen diagnosis of pancreatic disease is difficult because no direct method of visualization exists and secondary signs must be employed. Thus an annular pancreas will narrow the duodenal lumen and produce a partial obstruction.

Pancreatic stones are said to be very rare. The author, however, made a roentgen study of the pancreas in 1,000 cadavers without reference to the clinical diagnosis and found evidence of calcification (over 2 mm in diameter) in 81. Necropsy showed 55 to be cases of stone, 10 of calcification in fat necrosis and 16 of ossification in pancreatitis or fat necrosis. Size and shape were not characteristic, most of the concretions were sandy and single isolated stones were rare. Differen-

The author concludes with an interesting but brief commentary on the association of the etiology of spondylolisthesis with the anthropologic and ontogenetic development of the lumbosacral spine

PAUL W EYLER, M D

Spondylolisthesis Additional Variations in Anomalies in the Pars Interarticularis Maurice B Roche and Charles S Bryan Arch Surg 53 675-682, December 1946

The occurrence of spondylolisthesis in patients with unilateral spondylolysis and without rotation indicates the presence of other congenital defects to explain the mechanics In spondylolisthesis with bilateral spondylolysis and in spondylolysis, unilateral or bilateral, without spondylolisthesis, no problem is posed, and these conditions are discussed very briefly A case of unilateral defect on the left with slipping is presented, in which the presence of an intact right lamina of unusual length explains the mechanism A case of reversed spondylolisthesis without spondylolysis is shown, in this patient the neural arch was unusually short and almost vertical in position The author feels that in cases of slipping without spondylolysis or with a unilateral defect such factors should be investigated For a complete understanding of the exact nature of the anatomic variations, oblique as well as anteroposterior and lateral projections should be included in the roentgenographic study of disability low in the back In cases of unilateral congenital spondylolysis, without symptoms before injury to the lower part of the back, oblique views may reveal a recent fracture of the previously intact side In cases of questionable symptoms, stereoscopic views are valuable

[An illuminating article.—L G J]

LEWIS G JACOBS, M D

Diagnosis of Root Compression J E W Brocher Schweiz med Wchnschr 76 1325-1329, Dec 28 1946

Five types of root compression may be distinguished posterior disk hernia, destructive infection (spondylitis), osteolytic neoplasm, primary intraspinal tumor, and separation of the posterior margins of the vertebral bodies Since both require laminectomy differentiation between intraspinal tumor and disk hernia is of little importance, but it is very important to distinguish between these and other conditions Of the positive or suggestive physical signs exacerbation of pain by sudden shaking of the back or by sudden elevation of the spinal fluid pressure (as in coughing, sneezing, laughing or defecation) is important Hyperextension in plaster will relieve this in disk herniation and at times in spondylitis, but not in intraspinal tumor Pain and muscle spasm may result in a characteristic posture Palpation of the spine is important since it may localize a sudden reversal of curve Stiffness on motion and local spasm are important, especially if hyperextension is painful Positive neurologic findings are useful, but their absence is of no significance Hypesthesia and reflex changes are especially important The course of the disease must be considered, a sudden beginning, with a trauma as a rule, a month- to year long course, and refractoriness to therapy are typical The spinal fluid will show elevation of the albumin in cord tumor and in 50 per cent of disk hernias The most consistently positive findings are obtained by iodide myelography—up to 90 per cent according to most authors

Air or carbon dioxide are not advised Study of the sacroiliac joints must not be neglected, since disease here may cause similar symptoms Oblique views of the spine to exclude spondylolysis and to study the posterior articulations are necessary Roentgen findings must always be evaluated in the light of the clinical picture

LEWIS G JACOBS, M D

Arrest of Growth of the Epiphyses John T Hodgen and Charles H Frantz Arch Surg 53 664-674, December 1946

The arrest of epiphyseal growth to correct unequal length of the legs leads to better results with increased experience. Energetic handling and early operation are desirable Blount's operation, the use of removable staples to arrest the growth, is a marked technical improvement It is in determining the optimum time for operation that most difficulty is experienced The amount of discrepancy in length is first determined, best by use of x-ray, wood blocks to level the pelvis or a film showing pelvic tilt may be used, and teleroentgenography and slit scanography have been successfully employed When the shortening has been measured, the ratio (shortening present)/(expected growth) gives the percentage of growth to eliminate, and the proper epiphysis to correct this may then be chosen from standard tables giving the percentage of the limb growth contributed by each epiphysis Of 21 patients operated upon by these authors, 10 showed a gain, i.e., a decrease in discrepancy, of 75 to 100 per cent, 10 a gain of 25 to 75 per cent, and only 1 less than 25 per cent gain

LEWIS G JACOBS, M D

Fractures of the Os Calcis. Their Treatment by Tri-Radiate Traction and Subastragalar Fusion. R I Harris Ann Surg 124 1082-1099, December 1946

Management of fractures of the os calcis is difficult because (1) standardization of treatment is nearly impossible, (2) the technical problems involved in reduction of the fragments are complex and difficult, and (3) involvement of the subastragalar joint with late disability from pain on movement is frequent As in other fractures success in treatment is based on reduction of the fragments to as nearly perfectly normal relationship as possible. While restoration of the critical angle is an index of restoration of the fragments, of greater importance is the state of the posterior facet of the subastragalar joint

Harris distinguishes between simple and severe fractures of this bone. For severe fractures he recommends tri radiate traction supplemented by leverage with a Steinmann pin in certain cases Kirschner wires are passed (a) through the upper end of the crest of the tibia (b) through the posterosuperior angle of the os calcis, and (c) through the distal ends of the fifth and first metatarsals Tri radiate traction is applied and the results are checked roentgenographically If they are unsatisfactory, adjustments are made and the results rechecked When a lateral roentgenogram shows satisfactory restoration, the widening of the os calcis is reduced by molding pressure from either side From a study of the post reduction film, a decision is reached upon the necessity for subastragalar fusion The criterion for this decision is the degree of fragmentation and deformity of the articular surface of the posterior facet of the os calcis If the reduction is satisfactory, plaster is applied and the traction is removed as soon as this is thoroughly dried Cases which are judged

and local operation in 10 per cent. Of the 71 patients 21 died within three years. Four are alive but with evidence of the disease and 15 are alive and apparently well.

JOSEPH L. DIXON, M.D.

Multiple Myeloma: A Review of Fifty-Three Proved Cases. Edward D. Hayd and Frank J. Fleck. *J. A. M. A.* 133: 117-157, Jan. 15, 1917.

Pain was found to be the most frequent clinical manifestation of multiple myeloma. Nearly three-fourths of the authors' 53 patients had multiple bone lesions and a small number had elevated serum protein. Bence Jones protinuria was present in slightly over half of the cases. Twelve per cent showed no bone abnormality, while 9 per cent showed osteoporosis alone. A sixth of the group had pathological fractures of bones other than vertebrae; twelve per cent had tumor formation. Other significant findings were evidence of renal dysfunction, excessive renal excretion, anemia, hyperleukemia, myeloid immaturity myeloma cells in the peripheral blood and epistaxis. The above findings are all carefully discussed and correlated.

Diagnosis should be confirmed by sternal puncture

vertebral column would fall into this group and the author is of the opinion that the posterior spine should be fused in these in order to provide greater stability for the back. He believes anterior fusion is capable of providing permanent relief in mild cases of pure intervertebral disk disease.

The roentgenographic aspects of spondylolisthesis are reviewed and mention is made of the pseudospondylolisthesis of Jungblum, which is characterized by the dislocation of one vertebra upon another when there is not a preceding intense trauma or a separate neural arch. In these cases osteoarthritic change may be present at the apposing vertebral surfaces and the articular line of the inferior small articulation of the displaced vertebra tends to be more horizontal than in the other articular lines. Most of these cases have been at the level of the fifth lumbar vertebra.

Comment on reverse spondylolisthesis is also included as is mention of a few cases associated with scoliosis. The progression of the characteristic deformity of spondylolisthesis was observed and the conclusion reached that further slipping may occur at any time except in cases in which a buttress or osseous synostosis is present but that cases of progression after puberty are of infrequent occurrence.

The author concludes with an interesting but brief commentary on the association of the etiology of spondylolisthesis with the anthropologic and ontogenetic development of the lumbosacral spine

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Air or carbon dioxide are not advised. Study of the sacroiliac joints must not be neglected, since disease here may cause similar symptoms. Oblique views of the spine to exclude spondylolysis and to study the posterior articulations are necessary. Roentgen findings must always be evaluated in the light of the clinical picture.

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suitable for sublingual fusion are created upon ten days after the primary reduction of early fusion waves then and it is possible early return to work. Harris agrees with this plan of treatment as satisfactory.

ELLIS W. COOPER, M.D.

Talonvicular Synostosis. Fred C. Hoel, on South M. J. 39, 910-911, December 1916.

The author reports a case of congenital bilateral talonavicular synostosis in a woman of thirty with symptoms first appearing after her last weight examination of a sister of the patient showed an exactly similar condition. A daughter was found to have normal talonavicular articulation.

GYNCOLOGY AND OBSTETRICS

Use of Radiology in Predicting Difficult Labor. J. C. and Mrs. J. O. & Cyrene Brit Emp 53, 187-197, Dec. 30, 1916, 54, 25-31, February 1917.

The title of the two lectures appearing in this group abstracts of the first and second lectures on radiology in gynecology and obstetrics.

For often as you read the literature there has been a lack of cooperation between the radiologists and the obstetricians so that neither fully appreciated the needs and desires of the other. As a result there was an "I believe still a long way to go" in the place of what might be termed a "revelation" in the history of the radiograph with the obstetrician's aid. The author rather than a long period of time, even though the distance of the anterior pelvis or the pelvic inlet and the fetal head of the mother. Although the author is well known to be a fully trained radiologist, he has actually taken over the radiological examination in order to evaluate for himself the various methods of pelvimetry. He does not, however, recommend this dual role to obstetricians in general. His studies now cover nearly 500 cases.

Interestingly enough the author suggests that all projections of the pelvis should be made at a distance of not less than 1 foot. If a bulky diaphragm is used 1 1/2 feet should be a minimum. The use of the erect position for the lateral projection is advised, and an ingenious rack is described for immobilizing the patient rather comfortably. A support has also been devised for the patient for the supero-inferior projection. The method of recording the marker on the supero-inferior projection of the pelvis is rather ingenious, a half circle wire loop is used to hold the marker behind the patient tilted at the same angle as the sacrum. The corrected centimeter scale is incorporated on the film with the curved wire.

The pubic arch is projected onto the film by a postero-superior antero-inferior projection with the patient sitting on a specially constructed box with an oblique slot to hold a cassette for a 6 X 4 inch film. This it is believed, gives a more accurate recording of the subpubic arch.

Cephalometry, when the fetus is in the breech position is done by incorporating a scale measurement on a tangential view of the fetal head, which is located by palpation. If one is to estimate the growth of the fetal head after the film is made in relationship to the projected date of delivery, one should consider that the head grows about 2 mm. per week. The effect of molding on the biparietal diameter is discussed.

To this first lecture the author appends an addendum

rebutting a criticism of brim pelvimetry by Heyns (J. Obst. & Gynaec. Brit Emp 52, 148, 1915).

The second lecture—Forecasting the Course of Labor—is introduced by an enumeration of six features of a good obstetric pelvis, and a discussion of the Nicholas series of measurements and Thomas' early work on pelvic charts. The author then proceeds to his own graph method which he designates the "focal point" of the two papers. This is based on a consideration of the anteroposterior and transverse diameters of the brim pelvic cavity at the level of the sacral spines and the outlet. The concept is of the diameters of the brim is somewhat at variance with the orthodox teaching. He believes that the promontory of the sacrum is not usually the important posterior landmark. Instead he takes as the anteroposterior diameter the shortest distance between the upper and lower margins of the symphysis pubis and the nearest part of the sacrum as a rule the junction of the first and second sacral segments as a point between that and the promontory. The transverse diameter he defines as that which intersects the conjugate of the brim at the midpoint. The lower interspinous distance of the pelvic cavity is taken from the nearest part of the lower margin of the symphysis pubis to the tip of the sacrum or if the sacrum is full to the sacrum to the first free interspinous point. The inlet sometimes he discovered clinically rather than by x-ray examination alone. The transverse diameter of the pelvic cavity is reckoned as the distance between the sacral spines. The outlet is best estimated by measuring the subpubic angle and using this measurement in conjunction with the posterior sagittal dimension of the outlet.

In the evolution of the graph method three types of graphs were prepared one for the brim, one for the cavity and one for the outlet. In each the anteroposterior dimension were marked vertically and the transverse dimensions horizontally. By pin pointing a spot on each of the three graphs the main facts regarding the size and shape of any particular pelvis could be recorded. Separate sets of three graphs were made for each size of the fetal head from 9.0 to 9.9 cm. biparietal diameter that is ten sets of graphs in all. All the data from some 500 cases with the criteria of easy spontaneous delivery and difficult labor is judged clinically were spotted on these graphs. Having marked out the dividing line on each individual chart it was then possible to combine the charts and to draw up a single set of three charts showing the dividing lines for easy and difficult deliveries for each size of fetal head. These are now the key charts on which it becomes an easy matter to pinpoint any pelvis and to determine its obstetric value relative to the estimated size of the fetal head.

The series of cases on which these graphs are based included a large number with a high head at term or other clinical evidence of disproportion. From some points of view this is an advantage but the excessive proportion of borderline cases makes the material unsuitable as a fair test of the value of the graphs in indicating the probable course of labor in the general run of cases. A number of cases of dystocia not due to cephalopelvic disproportion were also included—a group in which there is no way of absolutely predicting the course of labor.

The prediction of dystocia is surest when a fault is revealed in the brim graph and considerable weight should therefore be given to such evidence.

The following blind spots in the graph technic are enumerated (1) a high inclination of the pelvic brim which, if there is already some tendency to disproportion, influences the prognosis unfavorably, (2) lack of a normal full curve of the sacrum from above downwards, giving a lessened posterior sagittal diameter and thereby accentuating any tendency to disproportion, (3) malposition of the head

Radiology has been found to be especially useful under the following conditions (1) a high head at term and suspected pelvic contraction, (2) abnormal or prolonged labor, (3) postmaturity and prematurity (cephalometry helps in predicting the degree of maturity of the fetus more than any other single criterion), (4) breech presentation when the head cannot be engaged directly against the pelvic brim, (5) suspected hydrocephalus, (6) necessity of deciding whether a patient can be safely delivered at home, (7) previous difficult labor, (8) fear of obstetric delivery

Certain criticisms which have been brought against obstetric radiology are refuted and the paper concludes with the statement that good obstetrics requires sound clinical judgment which depends on observation and appreciation of diverse clinical features, a part of which is radiology

SYDNEY F THOMAS, M D

The Pelvic Survey Herbert Thoms Yale J Biol & Med 19 171-179, December 1946

This article is truly a pelvic survey in so far as it defines the points of view of the obstetrician and the radiologist and correlates the two in arriving at a useful method of applying pelvic measurements from roentgenograms to the clinical survey. It is pointed out that it is necessary not only to make the measurements, but also to relate these measurements to the shape of the pelvis and the clinical measurements and appearances.

The author quotes from a previous article (Thoms and Schumacher Am J Obst & Gynec 48 52, 1944)

'we wish to observe that midplane pelvic contraction as indicated by shortening of the transverse diameter combined or not with shortening of the midplane anteroposterior diameter is definitely associated with increased operative intervention during labor. When the midplane is 9.5 cm. or less and other diameters remain in average limits according to this study the incidence of intervention was 45.2 per cent. When midplane anteroposterior shortening was also present, operative incidence was 65.0 per cent.'

The essential diameters of the pelvic inlet are

I The anteroposterior diameter, extending from a point on the upper posterior surface of the symphysis pubis 1 cm. from its superior border, posteriorly to the anterior surface of the sacrum to the point where the iliopectineal lines would meet were they extended

II The transverse diameter being the widest distance separating the iliopectineal lines

III The posterior sagittal diameter being that portion of the anteroposterior diameter which lies posterior to its intersection with the transverse diameter

The essential diameters of the midplane are

I The anteroposterior diameter, extending from the lower posterior border of the symphysis posteriorly at the level of the ischial spines to the lower third of the sacrum, usually falling at or near the junction of the fourth and fifth sacral segments

II The transverse diameter, being the narrowest distance separating the ischial spines.

III The posterior sagittal diameter, that part of the anteroposterior diameter which lies posterior to its intersection with the transverse diameter

For achieving these measurements two views of the pelvis are recommended the conventional anteroposterior projection of the pelvis (which really amounts to a projection looking down into the pelvic space) and a true lateral projection made in the upright position. Both films are made at a distance of 36 inches. In the anteroposterior projection, the perforated grid is superimposed on the film at the same level as the symphysis. The importance of the subpubic angle is belittled. The medical judgment of the outlet is in the author's experience more useful than any attempt at a judgment of the adequacy of the outlet from the roentgenogram.

In conclusion, the author states, "It must be re-emphasized that, even with the availability of this increased knowledge of pelvic morphology and dimensions, the problems of childbirth still remain manifold and complex and must be viewed in their entirety in the scientific conduct of labor."

SYDNEY F THOMAS, M D

THE GENITO-URINARY SYSTEM

A New Technique of Perirenal Air Insufflation Francisco J Barquin J Urol 57 1-14, January 1947

The author conceived the idea of inserting the needle for perirenal air insufflation through the line of incision used for exploration of the kidney. The patient is placed in the usual lateral position for exploration of the flank, with maximum elevation on a Pilet support to open the costo-iliac space and displace the peritoneum and intestines. After the usual sterile preparations, a large spinal puncture needle is introduced through the skin at the junction of the proximal two fourths of a line drawn from the costovertebral angle to the anterior superior iliac spine. The needle is directed upward and inward toward the spine and diaphragm and inserted until it touches the kidney at which time the hub of the syringe will move up and down with inspiration and expiration.

Before injecting each syringe of air the blood pressure is taken. The author has found a drop of blood pressure in every case, sometimes reaching a maximum of 70 mm. systolic, but this is easily controlled by central and peripheral stimulants. The diastolic pressure does not usually fall more than 5 to 10 mm. It is believed that a fall in systolic pressure may be responsible for some of the serious accidents reported by certain urologists as due to gas embolism.

Before the first air is injected 5 c.c. of normal saline are introduced through the syringe to separate the kidney cortex from the tip of the needle. Aspiration is then done to make sure that a blood vessel has not been entered. Thirty cubic centimeters of air are injected at a time for a total of 600 to 900 c.c., according to the patient's tolerance.

Fourteen case reports are presented, with good reproductions of roentgenograms made following air insufflation.

VERN W RITTER, M D

Differential Diagnosis of Surgical Renal Lesions. Meredith F Campbell Am J Surg 72 786-799, December 1946

The differential diagnosis of surgical renal lesions is here considered including chronic pyelonephritis, in-

ected hydronephrosis, renal tuberculosis, calculus, tumor, acute renal infection and congenital malformation. Diagnosis is difficult since practically all renal diseases may present a similar clinical picture. In all cases, careful urinalysis of a properly collected specimen is of greatest diagnostic importance. Cure of urosurgical conditions implies a restoration of urine to normal, including sterilization of the urine as attested by at least two negative cultures.

In *surgical non tuberculous renal infections* the usual lesion is an interstitial suppurative nephritis which may exist alone or as a complication of a stone or obstruction. In acute renal infections failure of intensive medical therapy to bring marked improvement in three to four days calls for complete urologic examination. This will usually reveal infected hydronephrosis, generally due to pelvic outlet or upper ureter blockage by stone, stricture, malposition, aberrant vessel, or perirenal abscess. Also there may be a renal carbuncle or a pyemic kidney.

Any retroperitoneal edema producing lesion, as a perinephric abscess, will roentgenographically obscure the ipsilateral psoas muscle shadow and usually show lumbar curvature away from the lesion due to compensatory spasm of the ipsilateral erector spinae group. This picture along with acute intra abdominal disease with unilateral renal area tenderness and a history of recent cutaneous infection, suggests perinephric abscess. Yet retrocecal appendicitis and edema may produce the same picture and would be favored by the urographic demonstration of a normal upper urinary tract. Also the same picture is presented by the rare renal infarction, or thrombosis, but this occurs most often in infants or the young and is associated with more acute onset and variable shock and prostration.

Chronic surgical urinary infection with persistent pyuria despite medical therapy demands urologic examination which often discloses chronic pyelonephritis complicated by or associated with infected hydronephrosis, ureteral obstruction, calculus, tuberculosis or malformation. In half of these cases reflex or toxic gastro-intestinal symptoms lead the diagnosis away from the basic urinary tract lesion. With these vague symptoms the urinary tract must not be overlooked.

The multiple causes of *hydronephrosis* stem from lesions anywhere in the urinary tract from calyx to meatus and include strictures (congenital and inflammatory), stones, adjacent abscesses or tumors, intrinsic muscle spasm, mucosal folds, vascular obstruction and neuromuscular vesical disease. The need for thorough urologic examination to identify the site and

parenchymal ulceration commonly with cavitation and heavy calcium infiltration, and sometimes perirenal disease as well.

Pain in the renal area or along the course of the urinary tract together with gross or microscopic hematuria and pyuria, are classic symptoms of renal disease. A large immobile pelvic stone may be 'silent'. Urography usually establishes the diagnosis.

Painless fresh hematuria most often means disease in the adult and nephritis in the child. Accurate pre-operative diagnosis of renal tumor requires urography. Retrograde pyelography is here preferable since changes in the finer pelvic markings are of paramount importance. The pelvic outline is usually distorted with compression and elongation of the calices. Filling defects sometimes occur in the pelvis from papillary growths.

Surgically, the most important renal malformations are agenesis, hypoplasia, reduplication, ectopia, fusion, cystic kidneys and abnormal motility. Abdominal pain, a palpable mass, and abnormal urinalysis direct attention to the urinary tract. Renal malformations often accompany major deformities of the external genitalia. In all these malformations, the correct diagnosis can almost always be made by urography. The anomalous kidney is more prone to disease than the normal one. Congenital absence and aplasia should be recognized, so that the solitary functioning kidney is not unnecessarily removed. Roentgenograms should be made with the patient in the Trendelenburg position as well as upright to detect abnormal motility. In polycystic disease the pyelogram shows a notable tendency to crescent like dilatation of the major calices.

DOUGLAS R. SAGLE, Jr. M.D.

Non-Fused Pelvic Kidney. A Study of Nine Cases.
Ralph L. Dourmashkin. Urol. & Cutan. Rev. 50: 712-719. December 1916.

Nine cases of non fused kidney occupying either the true pelvic or the lumbo ilio pelvic position are recorded. Concerning the roentgen diagnosis of this anomaly the author says that frequently the pelvic kidney is not demonstrable on a plain film or even in an intravenous pyelogram either because the dye shadow is superimposed upon the pelvic bone shadow or because of poor dye elimination. In only 2 of the cases in this series did the plain film show a definite outline of a pelvic kidney. This anomaly should be suspected however in any case in which a plain film fails to show the normal renal silhouette.

to be differentiated from a ptosed kidney, renal agenesis, an abdominal neoplasm, diseases of the lower abdominal organs, and megaloureter

MAURICE D. SACHS, M.D.

THE BLOOD VESSELS

Unusual Venous Returns of the Lower Extremities
E. C. Baker. *Am J Roentgenol* 57: 50-55, January 1947

The venous channels which may be visualized in the normal venogram of the leg and thigh are described. The internal saphenous vein is the normal main channel for the superficial portion of the system. The tibial veins unite with the peroneal veins to form the popliteal, which becomes the femoral vein above the popliteal space. These are the deep channels. In the fossa ovalis the internal saphenous vein and the femoral vein unite to form the external iliac vein.

In acute block of the main deep physiological channel of the thigh the injected dye seeks numerous small veins below the site of the block. These veins form a

lacy network in the superficial tissues. Following such an acute block, nature gradually finds larger channels in the area of the block so that in a few weeks to several months certain main physiological channels are formed out of already existing veins, and these become the main channels for the blood stream in blocks of long duration. Usually the blood flow through these veins is now reversed and the injected dye extends outward from the region of the fossa ovalis through them to collateral circulation where normal upward channels are reached. Cases are presented, with illustrations, of acute deep block in the thigh, chronic deep block of the thigh with return through the pudendal circulation, chronic deep block with return through circumflex veins and with return through perineal veins and midsacral veins. Another case is shown in which a block occurred in the region of the fossa ovalis with partial return through the inferior gluteal vein.

When unusual types of return are visualized in the region of the fossa ovalis or upper thigh, it is concluded that this is conclusive proof of a deep block.

CLARENCE E. WEAVER, M.D.

RADIOTHERAPY

Results of Radiotherapy of Epibulbar Tumors at Radiumhemmet, Stockholm, 1920-1940. Harry Larsson. *Acta radiol* 27: 358-373, May 6, 1946.

During the period 1920-40, 66 cases of epibulbar neoplasms—i.e., neoplasms in the conjunctiva on the anterior side of the bulbus oculi—were treated. For the most part treatment was by surface application of a weakly filtered radium preparation but the more advanced malignant tumors received roentgen therapy in high dosage. "Plane preparations" of radium were used, containing 10 and 5 mg. of radium element, respectively. The radium sulfate is fused into a porcelain plate 1.0×1.0 or 1.0×0.5 cm. and the rays are filtered through 0.2 mm. of nickel or German silver.

Of 37 patients with growing epibulbar tumors which were without histologic or clinical evidence of malignancy, 30 were completely free of symptoms for five years or more after treatment. Of 7 neovascular tumors in which it was impossible to exclude malignancy histologically, 6 were symptomless after five years or more. In 5 of these cases extirpation of the tumor preceded irradiation. Of 14 patients with a histologic diagnosis of malignant melanoma, 7 survived five years or more after a combination of surgical and irradiation therapy. Two patients had papillomas of suspected malignancy, and one of these was free of recurrence at the time of his death from pneumonia five and a half years after treatment. Four of 6 patients with squamous-cell carcinoma were without symptoms for five years or longer.

The author considers preoperative irradiation the method of choice for localized epibulbar tumors with subsequent extirpation or a more radical surgical procedure only when there has been a radioresistant recurrence or the primary tumor has failed to regress.

Radiation injury to the eye occurred in 5 cases, 4 of which had received heavily filtered radium applications or roentgen irradiation. The one patient in this group who was treated by means of the superficial plane applicator was a one-year-old girl. The pea-sized nevus disappeared completely, but six years after treatment

clouding of the cornea occurred and was attributed to the irradiation.

ELIZABETH A. CLARK, M.D.

Case of Cancer of the Oesophagus, Alive and Free from Evidence of Tumour 6 Years after Roentgen Treatment. Folke Jacobsson. *Acta radiol* 27: 351-357, May 6, 1946.

A 58-year old man had experienced difficulty in swallowing for about a year before hospital admission. Roentgen examination revealed a tumor in the lower esophagus, shown by biopsy to be a squamous-cell carcinoma. Treatment was by roentgen irradiation, an estimated tumor dose of about 5,000 r being administered by cross firing through six fields in a period of thirty-five days. The patient tolerated treatment well and improvement was noted during the period of hospitalization. Cardiac symptoms with cardiac enlargement and pleural effusion developed within three months and were regarded as a radiation effect. Nevertheless the patient was alive and well without evidence of recurrence or metastases six years after treatment and with only mild cardiac disturbance. Esophagoscopy showed no evidence of tumor.

ELIZABETH A. CLARK, M.D.

Roentgen Therapy of Lung Tumors. Sordello Attili. *Radiologia (Rome)* 1: 81-85, 1945.

The author treated with roentgen therapy 25 primary lung tumors and 23 metastatic lesions of the lungs. Of the 25 patients with primary tumors, only 2 were well at the end of two years but the local symptoms and general well-being of the patients improved in 60 per cent of cases. Of the 23 with metastatic lesions, only 1 was still alive at the end of one year and only 5 were subjectively improved. The author used 180 kv., 10 ma. 0.5 mm. Cu plus 3.0 mm. Al, 200 to 300 r daily until a tumor dose of 4,000 to 8,000 r had been reached.

In view of his results Attili concludes that roentgen therapy should be tried in those patients with primary lung tumors which are not susceptible to surgical treat-

ment because of the subjective improvement. If the lesions are metastatic, such an improvement can be expected only in a limited number of cases.

CESARE GIANTURCO M D

Regression of the Changes of Pulmonary Osteoarthropathy Following Treatment of the Primary Lung Conditions. Adamo Grillo Radiologia (Rome) 1 21-45 1945

The author reports 3 cases of pulmonary tumors with osteoarthritic manifestations: severe periosteal reaction, and hypertrophy of the phalangeal soft tissues. Two of the patients were given roentgen therapy and one underwent lobectomy. Following treatment the osteoarthritic and soft tissue alterations underwent notable regression in all cases.

CESARE GIANTURCO M D

Effect of Estrogenic Hormone on Advanced Carcinoma of the Female Breast. Julian B. Herrmann, Frank E. Adair, and Helen Q. Woodard. Arch Surg 54 1-9 January 1947

Seventeen patients with carcinoma of the breast (13 primary, inoperable, 4 recurrent) were treated by oral administration of ethinyl estradiol, a synthetic estrogenic hormone, receiving daily doses of 0.15 to 0.7 mg over periods of two to eleven months. Eight died (one of intercurrent disease) within eighteen months, 7 including 2 with pulmonary metastases showed some clinical improvement, and 1 showed cytologic changes of degeneration in the tumor without clinical improvement. Uterine bleeding was induced in 8 patients amounting to a serious hemorrhage in 1. A favorable response occurred predominantly in women past 60, in younger women, especially in those not in the menopause the effects were deleterious.

LEWIS G. JACOBS M D

cent obtained a five year cure 16.6 per cent a ten year cure.

3 Of 89 patients treated with x rays and radium 28.0 per cent obtained a five year cure 23.0 per cent a ten year cure.

4 Of 20 patients treated with surgery alone, 35 per cent obtained a five year cure 50.5 per cent a ten year cure.

5 Of 16 patients treated with radium and surgery 86 per cent obtained a five year cure 81.8 per cent a ten year cure.

6 Of 96 patients treated with x rays and surgery 77.0 per cent obtained a five year cure 65.0 per cent a ten year cure.

7 Of 11 patients treated with x ray radium and surgery, 66.6 per cent obtained a five year cure 60.0 per cent a ten year cure.

8 Twenty-one patients received no treatment.

Additional tables are presented showing the histologic grading and clinical grouping of the cases treated.

The authors conclude that preoperative x ray therapy has proved to be a valuable adjunct to total hysterectomy and bilateral salpingo-oophorectomy. It clears up uterine infection, reduces uterine size, and decreases pelvic hyperemia. Radium likewise gives good results, but on the basis of the available data the relative merits of x ray versus radium cannot be accurately stated.

PHILIP W. DORSEY M D

Dysgerminoma of the Ovary. A Review of Eleven Cases of Proved Tumor, with Special Reference to Radiosensitivity. Robert D. Morison and Arthur L. Desjardins. Am J Roentgenol 57 54-60 January 1947

In general the majority of investigators believe that dysgerminoma is derived from embryonic germ cells as a result of some undetermined stimulus. A few believe

offers the best prospect of longevity is surgical removal of the tumor plus adequate postoperative therapy. Four cases of dysgerminoma of the ovary are reported in detail in this paper. CLARENCE E. WEAVER, M.D.

Carcinoma of the Vulva. Results of Treatment and Effect of Special Factors on Results. Frank R. Smith and Robert S. Pollack. Surg., Gynec. & Obst. 84: 78-84, January 1947.

Two hundred and twenty-eight histologically proved cases of carcinoma of the vulva treated at the Memorial Hospital, New York, during a twenty-year interval (1926-45) are reviewed as to results of treatment and the effect of special factors on results.

The authors divide their cases into three general groups: (1) cases without involvement of inguinal nodes, (2) cases with inguinal nodes involved but operable, and (3) inoperable cases with inguinal nodes fixed or immobile. Their statistics show a marked difference between results in the early low-grade lesions and those which have become metastatic and invasive. They indicate that those patients who have received vigorous and prompt treatment do the best. They are in favor of vulvectomy with at least a bilateral superficial groin dissection in all cases suitable for surgery. Although only a relatively small proportion of the operable cases were treated by radiation, the authors are of the opinion that x-ray and radium are inadequate for treating either the primary or any locally metastatic lesion.

The authors state that carcinoma of the vulva accounts for only 4 per cent of all cancers of the female genital tract. In their series the youngest patient was 27, the oldest 89, with the majority between 50 and 69 years of age. Eighty-four per cent of the patients had an epidermoid type of carcinoma. The absolute five-year cure rate was 26 per cent.

MARLYN W. MILLER, M.D.

Carcinoma of the Bladder. A Classification of Epithelial Tumors and a Study of the Effects of External Radiation. Fletcher H. Colby and Ronald C. Sniffen. J. Urol. 57: 133-139, January 1947.

A microscopic and clinical study of bladder carcinoma is presented in an effort to correlate the histology of these tumors with response to x-ray therapy. The Massachusetts General Hospital classification and Broders' method of grading were used. The tumors being divided into papillary and non-papillary: the former graded 1A, 2A, and 3A and the latter 1B, 2B, and 3B, according to malignancy. The histologic factors upon which the grading is based are described in detail.

The morphology of 26 tumors observed remained constant throughout treatment except for one or two papillary lesions which invaded the bladder wall and became non-papillary. These tumors were observed before and after therapy for histologic changes. The authors conclude that the diagnosis of "radiation reaction" on a histologic basis is not practicable, as two such diagnoses were made prior to therapy and in the remaining tumors there was no constancy in post-irradiation features.

A total of 130 tumors of the bladder treated with a 1,200 kv. unit were studied. Some were given 7,200 to 8,400 r in doses of 300 to 400 r per treatment and some received 6,000 r in doses of 300 r per treatment. Additional courses of 2,400 r to 4,800 r were given in some

instances. It is not stated whether these are tumor doses or nmr doses.

One hundred and eleven cases were classified and graded. In these cases no definite correlation was found between histology and response. Papillary and non-papillary tumors responded equally well, showing regression in one-third of cases, while symptoms were relieved in about one-half. PAUL R. NOBLE, M.D.

Results of Treatment with Radiotherapy in Carcinoma of the Prostate. Sven Hultberg. Acta radiol. 27: 339-350, May 6, 1946.

The author has analyzed the cases of prostatic carcinoma treated by irradiation at Radiumhemmet between 1929 and 1940. Of the total of 167 cases, 107 were inoperable and were treated by irradiation alone, 46 were referred for postoperative irradiation, and 14 patients were seen only after recurrence or metastases had developed. Seventy cases received roentgen irradiation, 25 received telradium therapy, and 65 a combination of the two. Of the remainder 3 received such small amounts that no evaluation can be made and 4 were treated with implantation of radium needles. In no case was an attempt made at castration.

The percentage of five-year survivals was appreciably higher for the group receiving telradium therapy either alone or combined with roentgen irradiation. In evaluating this survival rate, the author stresses the fact that, despite careful attempts to protect the testicles during telradium treatment, they probably received a dose of about 350 to 500 r, while with roentgen therapy the dosage to the testicles was negligible. In general also, the dose to the prostate was greater with telradium.

In 105 patients metastases were present. Of the 82 patients with skeletal metastases the majority experienced relief of pain from roentgen therapy. The period of good palliative result varied from a short time to as long as two years in a few patients. The average duration of survival after the discovery of metastases was 12.9 months. ELIZABETH A. CLARK, M.D.

Three Cases of Testicular Tumor. John A. Taylor. J. Urol. 57: 175-184, January 1947.

Three rather unusual examples of testicular tumor are presented, in which a combination of surgery and roentgen therapy was used and long-term survivals were achieved. The pathological aspects are documented in detail, but only scant descriptions are given of the roentgen technique. Inguinal excision with pre-operative and postoperative roentgen irradiation is recommended as assuring the best prognosis in such cases.

The first patient had a seminoma of the right testis discovered incidentally in an examination for sterility. Five years after orchiectomy and postoperative roentgen therapy the opposite testis was found to be involved. A diagnosis of seminoma was again made and similar treatment was given. The patient is reported to be in good health nineteen years after the first operation. Testosterone was administered periodically following the second orchiectomy, and with gratifying effects.

In the second case five months after operation and postoperative irradiation for a teratoma of the left testis a metastatic mass was found in the abdomen. This disappeared following irradiation. Twelve years later a seminoma was discovered in the remaining

ment because of the subjective improvement. If the lesions are metastatic, such an improvement can be expected only in a limited number of cases.

CESARE GIANTURCO, M D

Regression of the Changes of Pulmonary Osteoarthropathy Following Treatment of the Primary Lung Conditions. Adamo Grilli. *Radiologia (Rome)* 1 21-45 1945

The author reports 3 cases of pulmonary tumors with osteoarthritic manifestations, severe periosteal reaction, and hypertrophy of the phalangeal soft tissues. Two of the patients were given roentgen therapy and one underwent lobectomy. Following treatment the osteoarthritic and soft-tissue alterations underwent notable regression in all cases.

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Effect of Estrogenic Hormone on Advanced Carcinoma of the Female Breast. Julian B Herrmann, Frank E Adair, and Helen Q Woodard. *Arch Surg* 54 1-9 January 1947

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LEWIS G JACOBS, M D

Corpus Carcinoma. A Study of Three Hundred Twenty-Two Cases. Norman F Miller and Charles W Henderson. *Am J Obst & Gynec* 52 894-900, December 1946

A comparative study is presented of 322 cases of corpus carcinoma treated by various methods. A "preferred program" was followed which was instituted in 1931 based on the following assumptions: (1) that elimination of the primary neoplasm could probably best be achieved through complete surgical extirpation of the entire uterus, tubes and ovaries; (2) that, theoretically, supplemental irradiation should be most beneficial when given prior to surgery, causing widespread damage to cancer cells, minimizing manipulative spread at operation, and causing some obliteration of the lymphatics. Since radiation was not depended upon for the destruction of the primary lesion but for its damaging effects on the outlying cancer cells, it was decided that x-ray therapy followed by adequate surgery should be the treatment of choice. X-rays were preferred to radium in the belief that with the broader fields affected by x-ray, some damage to neoplastic cell masses in the tubes and ovaries might occur. During the fourteen and a half years that this program has been pursued the following results were obtained:

1. Of 37 patients treated with radium alone, 41.3 per cent obtained a five-year cure and 30 per cent a ten-year cure.

2. Of 32 patients treated with x-rays alone, 27.2 per

cent obtained a five-year cure, 16.6 per cent a ten-year cure.

3. Of 89 patients treated with x-rays and radium, 28.0 per cent obtained a five-year cure, 23.0 per cent a ten-year cure.

4. Of 20 patients treated with surgery alone, 53.3 per cent obtained a five-year cure, 50.8 per cent a ten-year cure.

5. Of 16 patients treated with radium and surgery, 86 per cent obtained a five-year cure, 81.8 per cent a ten-year cure.

6. Of 96 patients treated with x-rays and surgery, 77.0 per cent obtained a five-year cure, 65.0 per cent a ten-year cure.

7. Of 11 patients treated with x-ray, radium, and surgery, 66.6 per cent obtained a five-year cure, 60.0 per cent a ten-year cure.

8. Twenty-one patients received no treatment.

Additional tables are presented showing the histologic grading and clinical grouping of the cases treated.

The authors conclude that preoperative x-ray therapy has proved to be a valuable adjuvant to total hysterectomy and bilateral salpingo-oophorectomy. It clears up uterine infection, reduces uterine size, and decreases pelvic hyperemia. Radium likewise gives good results, but on the basis of the available data the relative merits of x-ray versus radium cannot be accurately stated.

PHILIP W DORSEY, M D

Dysgerminoma of the Ovary. A Review of Eleven Cases of Proved Tumor, with Special Reference to Radiosensitivity. Robert D Moreton and Arthur U Desjardins. *Am J Roentgenol* 57 84-90, January 1947

In general the majority of investigators believe that dysgerminoma is derived from embryonic sexual cells as a result of some undetermined stimulus. A few believe with Ewing that the tumor is an atypical teratoma, other workers accept Fischel's (Ztschr f d ges Anat (Abt 1) 92 34 1930) theory according to which the origin of the lesion is related to totipotential mesenchymal cells.

Ewing (Neoplastic Diseases, Philadelphia, W B Saunders Co 4th Ed 1940 pp 661-662) wrote: "It is a malignant radio-sensitive, cellular tumor occurring at rather early ages, lacking hormonal effects, composed of large polyhedral cells of embryonal type and lying in a loose stroma containing many lymphocytes." The prognosis is relatively good in those instances in which the neoplasm is unilateral, encapsulated and non-adherent. Results of recent studies have shown that dysgerminoma may be associated with an excess of anterior pituitary-like substances in the urine.

Since the tumor ranks next to lymphoblastoma in radiosensitivity and since treatment with roentgen rays generated at high potentials may injure unaffected abdominal structures, the treatment in the authors' series has been carried out largely with roentgen rays generated at 130 kv (constant potential) usually filtered through 6 mm of aluminum. Four anterior (abdominal) fields which extend from the xiphoid cartilage to the pubic bone are used as well as four corresponding posterior fields. The left supraclavicular space is also irradiated. The surface of each field receives 540 r in air. The treatment is repeated in a month. Subsequent treatment is governed by the results of periodic examinations. The treatment which

previous menstrual period and intercourse eliminated during this time. It is of interest to note that the depth dose as administered by both these authors is approximately 120 r to the ovaries and about 180 r to the pituitary—S F T J SYDNEY F THOMAS, M D

A Tri-electrode Standard Air-Ionisation Chamber for Roentgen Ray Measurements in r-Units R Thoraeus Acta radiol 27 451-460, May 6, 1946

The author describes in detail a modification of his previous standard air ionization chamber (Acta radiol Supplement 15, 1932). The new instrument makes use of the cylindrical chamber, but consists of a tri-electrode within the electrostatic shield. The two compartments are separated by a 3 mm lead plate to eliminate the effect of scattered irradiation from the simultaneous irradiation on the two sides. By means of various connections, the new instrument can be used to advantage in measuring half-value layers and calibrating secondary standards and commercial dose meters. After extensive tests, measurements were found to compare favorably with those of the old type and the margin of error in r was about 10 per cent.

ELIZABETH A CLARK, M D

RADIOACTIVE ISOTOPES

Radioactive Iodine Therapy Effect on Functioning Metastases of Adenocarcinoma of the Thyroid. S M Seidlin, L D Marnelli and Eleanor Oshry J A M A 132 838-847, Dec 7, 1946

Previous studies of the effect of radioactive iodine upon thyroid carcinoma metastases have shown discouraging results. Only those metastases which microscopically show well differentiated tumor will consistently demonstrate sufficient uptake of iodine for treatment to be effective. This report covers studies of the therapeutic effect of radioactive iodine in one case of metastatic carcinoma of the thyroid in which all demonstrable metastases were shown to pick up radioactive iodine. The preparation used contained a mixture, in varying proportions of the two isotopes I^{130} (half-life 12.6 hours) and I^{131} (half-life 8 days). Both emit beta rays, which produce intense ionization within a few millimeters of tissue, as well as gamma rays which cause a negligible amount of ionization in the body and are sufficiently penetrating to be readily detected by an external Geiger counter.

The patient, a male aged fifty seven, had had a thyroidectomy for substernal goiter in 1923 at the age of thirty. The histologic diagnosis was malignant adenoma. He had had no thyrotoxicosis but only pressure symptoms from the mass. No signs of hyperthyroidism developed postoperatively and the patient was clinically well for fifteen years. Typical symptoms of thyrotoxicosis then developed, with severe pain in the lower back radiating down the legs. A small pulsating tumor was found in the mid line of the back at the level of the twelfth thoracic vertebra. Radiographs showed no osseous lesions. A laminectomy in 1939 revealed metastatic adenocarcinoma of the thyroid. The basal rate preoperatively was plus 40 per cent and post-operatively a thyroid crisis developed. Later exploration of the thyroid area showed no thyroid tissue either normal or malignant. Symptoms and signs of hyperthyroidism increased in the following two years and in December 1941 the basal rate was plus 45 per cent.

Radiographic study showed evidence of metastases to the lungs, upper part of the right femur, the left second rib, and the left ilium. High-voltage roentgen therapy for a total of 4,060 r over the dorsolumbar area and 3,180 r over the right femur produced no relief from pain.

In 1942 the patient still had pain and evidence of hyperthyroidism. Lugol's solution gave temporary amelioration for several months and then lost its effectiveness. The bone lesions continued to grow and pain persisted. Another course of roentgen therapy was given (3,260 r over the right femur and 1,985 r over the left pelvis), with no relief of pain.

In March 1943 a tracer dose of radioactive iodine was given orally in the form of sodium iodide in water. Geiger counter measurements revealed iodine retention by all known lesions and in two previously unsuspected ones. The first course of radioactive iodine therapy was administered between May and August 1943—a total of 102 millicuries of the 12.6 hour isotope and 20.5 millicuries of the 8-day isotope. The estimated radiation dosage to the tumors was 10,600 equivalent r, and that for the blood was 70 equivalent r. Fractionation of dosage allowed study of the effects on the leukocyte count. After one dose of 40 millicuries of the 12.6 hour isotope, the count dropped from 5,510 to 2,900 in one week, but returned to normal in ten days, even though an additional dose of 35 millicuries was given while the count was low.

The patient gradually improved and by November 1943 the pains diminished, the basal rate dropped to about plus 20 per cent, and there was a weight gain of about 15 pounds. No growth of metastases could be demonstrated. Dissection biopsy of a metastasis of the left second rib at this time provided material for radioautographs, determination of the amount of radioactive iodine per gram, and microscopic study. It was found that the position of the radioactive iodine in the tissue, as shown by radioautographs of thin sections, corresponded exactly with the active cellular areas as shown microscopically. It was estimated from these studies that the apparent tumor weight in the patient was 312 gm. The histologic study confirmed the diagnosis and showed the evidence of cellular destruction as well as residual activity.

In 1944 the patient was given a course of thiouracil therapy to check further on the functional nature of the metastases. This produced a striking remission of the thyrotoxicosis with recurrence on discontinuing treatment. Since then, two additional dosages of radioactive iodine have been given using the 8-day isotope. At the time of publication, the patient's general condition was good. He was practically free of pain and he moved freely about the hospital. His basal rate dropped to minus 27 per cent and has remained consistently low. Roentgenograms showed no progression of the metastatic lesions.

Four other cases of metastatic thyroid carcinoma without clinical hyperthyroidism have been studied with radioactive iodine and have shown selective localization in the lesions. Two of these are under treatment with radioactive iodine.

The reviewer believes this report to be of great significance in the therapy of this previously hopeless condition and regrets that space is not available to include many of the interesting details which are found in the original article. BERNARD S KALAYJIAN, M D

testis Like the original tumor, it was treated by surgery and x rays Two years after this another abdominal mass appeared but it too, yielded to irradiation The patient is well fourteen years after removal of the first tumor

In the third case the diagnosis was chorionepithelioma, with an associated acne and gynecomastia The involved testis was resected, radiation being given before and after operation The acne and gynecomastia were strikingly improved following treatment, suggesting an hormonal origin This patient is in apparent good health nine years after the tumor was discovered

Excellent photomicrographs of the lesions in all 3 cases are reproduced
PAUL W BYLER, M D

Boeck's Sarcoid (Sarcoidosis) Abraham Oppenheim and Robert S Pollack *Am J Roentgenol* 57 28-35, January 1947

Boeck's sarcoid is a generalized systemic disease with protean manifestations In its tendency to affect many organs, it simulates the lymphomatous diseases Chest roentgenograms show a bilateral symmetrical hilar enlargement In spite of this, there is a paucity of respiratory symptoms and physical signs Only one of the authors series of 42 patients showed bone changes It is concluded from this that bone changes are confirmatory signs only and that their absence should not preclude the diagnosis of Boeck's sarcoid Biopsy of peripheral lesions or lymph nodes can establish a definite diagnosis This was done in 27 of the authors' cases The tuberculin test was negative in 64 per cent of the series Involvement of the eye is comparatively common Thirty-four of the patients showed chest manifestations, and in 20 of these there were peripheral manifestations also In those showing chest lesions cough was the most prominent symptom Weight loss and dyspnea were the least common One patient had a gastric ulcer which proved on pathological examination to be Boeck's sarcoid Hodgkin's disease because of the close resemblance of the chest picture and other clinical features is the chief condition from which a differential diagnosis must be made

In cases where symptoms are present definite benefit is derived from the administration of small doses of roentgen radiation to the mediastinum and to peripheral nodes if the latter are palpably enlarged Of 24 cases thus treated in this series, 20 have been observed sufficiently long to indicate that the prognosis of Boeck's sarcoid is favorable Regression and complete disappearance of mediastinal and peripheral lesions have been noted after radiation therapy Symptoms when present have usually abated

CLARENCE E WEAVER, M D

Herpes Zoster Robert J Reeves and L Bradford Waters *Texas State J Med* 42 490-491, December 1946

After describing the incidence pathologic physiology, and diagnosis of herpes zoster, the authors discuss the various known methods of treating the disease Among these roentgen therapy has been found to be effective Kerchline is quoted (*Radiology* 22 372 1934) as having cured 90 per cent of 62 cases with a single treatment of 150 r through 3 mm Al at 30 cm distance Reeves and Waters used a technique similar to that of Tuggle et al (*Am J M Sc* 200 803, 1940 *Abst in Radiology* 37 257 1941) Fifty seven cases were treated The factors employed were 200 kv, 0.5 mm Cu and 1 mm Al

TSD 50 cm A daily dose of 200 r was administered for a total of 800 to 1,000 r It was noted that the patients showing an immediate increase in pain following the first treatment responded more readily to the therapy When symptoms had been of less than one week's duration, pain was relieved in seven to ten days When symptoms had been present for more than twenty-nine days before treatment was started, failure or only partial improvement was noted Of the total cases treated, 38 were cured 10 were improved and 8 were regarded as failures STANLEY H MACHT, M D

Treatment of Amenorrhea and Sterility by X-Ray Therapy Ira I Kaplan *New York State J Med* 46 2746-2752 Dec 15, 1946

Kaplan points out that in 1928 Rubin reported x-ray therapy as a means of relieving sterility associated with habitual amenorrhea In the same year, Hirsch (*Radiology* 7 93 1926) reported favorably on x ray treatment of ovarian hypofunction Other reports followed and the author has himself reported two previous series As a result of his treatment of 296 cases he is confirmed in his original view that radiation properly administered would be effective in a large number of cases of amenorrhea and sterility, without harm to mother or offspring The possibility of harmful effects upon future generations cannot be ignored but has not been demonstrated

Whether the x rays exert their effect directly upon the ovaries or upon the uterus or pituitary is not known The author discusses the observations of numerous investigators and reports illustrative cases supporting various views Without reaching any definite conclusion on the mode of action he concludes that no other treatment thus far devised including organotherapy, has yielded equally satisfactory results

The treatment factors are 200 kv 0.5 mm Cu plus 10 mm Al 50 cm distance The pelvic fields include right and left anterior and posterior and vary from 8 X 10 cm to 10 X 15 cm The pituitary field is limited to a 6 X 8 cm area The dosage was 50 to 75 r (measured in air) per treatment administered weekly for three weeks Each time the pelvis was treated the pituitary was given a dose of 75 r The series is not repeated

The indications for x ray therapy come only after every other method of treatment has failed and the gynecologist or consulting physician is qualified to judge that there is a possibility that roentgen therapy will be beneficial The younger the woman the better the chances of success if other indications are present

Of the author's 296 cases 70 were not traced Of the remaining 226 patients 55 failed to respond to treatment and in 171 menstruation was regulated Ninety of the latter group became pregnant, and 76 went to term (14 of those more than once) finally giving birth to 101 normal children In this series there were 2 cases of ectopic pregnancy and 10 miscarriages, 3 patients miscarried several times At the present time 6 patients are pregnant and 1 has had a therapeutic abortion Two patients were re-treated at their own insistence and gave birth to a second child

[Because of the known adverse effects of irradiation upon a developing fetus one must be certain that the patient is not pregnant In a recent article on x ray irradiation to promote ovulation, J O Haman (*West J Surg* 55 107 1947) points out that x rays should be given if possible within two weeks of the

previous menstrual period and intercourse eliminated during this time. It is of interest to note that the depth dose as administered by both these authors is approximately 120 r to the ovaries and about 180 r to the pituitary—S F T J SYDNEY F THOMAS, M D

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RADIOACTIVE ISOTOPES

Radioactive Iodine Therapy Effect on Functioning Metastases of Adenocarcinoma of the Thyroid. S M Seidlin, L D Marnell and Eleanor Oshry J A M A 132 838-847, Dec 7, 1946

Previous studies of the effect of radioactive iodine upon thyroid carcinoma metastases have shown discouraging results. Only those metastases which microscopically show well differentiated tumor will consistently demonstrate sufficient uptake of iodine for treatment to be effective. This report covers studies of the therapeutic effect of radioactive iodine in one case of metastatic carcinoma of the thyroid in which all demonstrable metastases were shown to pick up radioactive iodine. The preparation used contained a mixture, in varying proportions of the two isotopes I^{130} (half life 12.6 hours) and I^{131} (half life 8 days). Both emit beta rays, which produce intense ionization within a few millimeters of tissue, as well as gamma rays, which cause a negligible amount of ionization in the body and are sufficiently penetrating to be readily detected by an external Geiger counter.

The patient, a male aged fifty seven, had had a thyroidectomy for substernal goiter in 1923 at the age of thirty. The histologic diagnosis was malignant adenoma. He had had no thyrotoxicosis but only pressure symptoms from the mass. No signs of hypothyroidism developed postoperatively and the patient was clinically well for fifteen years. Typical symptoms of thyrotoxicosis then developed with severe pain in the lower back radiating down the legs. A small pulsating tumor was found in the mid line of the back at the level of the twelfth thoracic vertebra. Radiographs showed no osseous lesions. A laminectomy in 1939 revealed metastatic adenocarcinoma of the thyroid. The basal rate preoperatively was plus 40 per cent and postoperatively a thyroid crisis developed. Later exploration of the thyroid area showed no thyroid tissue either normal or malignant. Symptoms and signs of hyperthyroidism increased in the following two years and in December 1941 the basal rate was plus 45 per cent.

Radiographic study showed evidence of metastases to the lungs, upper part of the right femur, the left second rib, and the left ilium. High voltage roentgen therapy for a total of 4,060 r over the dorsolumbar area and 3,180 r over the right femur produced no relief from pain.

In 1942 the patient still had pain and evidence of hyperthyroidism. Lugol's solution gave temporary amelioration for several months and then lost its effectiveness. The bone lesions continued to grow and pain persisted. Another course of roentgen therapy was given (3,260 r over the right femur and 1,985 r over the left pelvis), with no relief of pain.

In March 1943 a tracer dose of radioactive iodine was given orally in the form of sodium iodide in water. Geiger counter measurements revealed iodine retention by all known lesions and in two previously unsuspected ones. The first course of radioactive iodine therapy was administered between May and August 1943—a total of 102 millicuries of the 12.6-hour isotope and 20.5 millicuries of the 8-day isotope. The estimated radiation dosage to the tumors was 10,600 equivalent r, and that for the blood was 70 equivalent r. Fractionation of dosage allowed study of the effects on the leukocyte count. After one dose of 40 millicuries of the 12.6 hour isotope, the count dropped from 5,510 to 2,900 in one week, but returned to normal in ten days, even though an additional dose of 35 millicuries was given while the count was low.

The patient gradually improved and by November 1943 the pains diminished, the basal rate dropped to about plus 20 per cent, and there was a weight gain of about 15 pounds. No growth of metastases could be demonstrated. Dissection biopsy of a metastasis of the left second rib at this time provided material for radioautographs, determination of the amount of radioactive iodine per gram and microscopic study. It was found that the position of the radioactive iodine in the tissue, as shown by radioautographs of thin sections, corresponded exactly with the active cellular areas as shown microscopically. It was estimated from these studies that the apparent tumor weight in the patient was 312 gm. The histologic study confirmed the diagnosis and showed the evidence of cellular destruction as well as residual activity.

In 1944 the patient was given a course of thiouracil therapy to check further on the functional nature of the metastases. This produced a striking remission of the thyrotoxicosis with recurrence on discontinuing treatment. Since then, two additional dosages of radioactive iodine have been given using the 8-day isotope. At the time of publication, the patient's general condition was good. He was practically free of pain and he moved freely about the hospital. His basal rate dropped to minus 27 per cent and has remained consistently low. Roentgenograms showed no progression of the metastatic lesions.

Four other cases of metastatic thyroid carcinoma without clinical hyperthyroidism have been studied with radioactive iodine and have shown selective localization in the lesions. Two of these are under treatment with radioactive iodine.

The reviewer believes this report to be of great significance in the therapy of this previously hopeless condition and regrets that space is not available to include many of the interesting details which are found in the original article. BERNARD S KALAJIAN, M D

Radioactive Isotopes J W Buchta. West J Surg 54 467-473 December 1946

Radioactive Iodine in the Study of Thyroid Physiology Use of Radioactive Iodine Therapy in Graves' Disease Saul Hertz and Arthur Roberts Ibid, pp 474-485

A Plan for Analysis of the Biologic Factors Involved in Experimental Carcinogenesis of the Thyroid by Means of Radioactive Isotopes Saul Hertz Ibid pp 487-489

The opening paper of this series, read before the American Association for the Study of Goiter in 1946 discusses the basic physics of isotopes and refers briefly to their employment as tracers in biological experiments. Hertz and Roberts report their results with internal irradiation by radioactive iodine in 29 cases of Graves' disease. By an analysis, over a long period of time of both their failures and successes it was found that

radioactive iodine, when given in the dosage range of 5 to 25 mc to uniodinized patients with Graves' disease, having goiters of 60 to 75 gm, is highly effective as a cure in about 80 per cent of cases. The use of ordinary iodine therapy after administration of the isotope is of advantage in the clinical care of these patients and in the economy and safety of the procedure. In 5 cases of the series subtotal thyroidectomy was done, and in all of these, hypometabolism resulted.

The authors consider that in typical cases of toxic goiter, 10 mc is a safe minimal dosage for adults. At 15 mc level, the percentage of cures is acceptable, at doses up to 25 mc the regularity of cures equals or surpasses that of current surgical treatment after iodine or thiouracil preparation.

The final paper in the group, by Hertz, places on record an experimental approach to the study of cancer of the thyroid with the aid of radioactive isotopes.

EFFECTS OF RADIATION

Fractures of the Femoral Neck Following Pelvic Irradiation Wendell P Stampfl and H Dabney Kerr Am J Roentgenol 57 71-83, January 1947

Osteoporosis is one of the more conspicuous microscopic findings in radiation osteitis and is extremely significant from the standpoint of irradiation fracture. Vascular absorption plays an important role and is brought about by the persistent dilatation of the vessels in the haversian and Volkmann's canals. Osteoclasts probably play a secondary part in the process. Zöllner (Strahlentherapie 70 193, 1941) believed that the osteoporosis following irradiation may be the result of a disturbance in the normal balance between resorption and production of bone on account of the sensitivity of osteoblasts.

Biopsies in 3 of the 12 cases presented by the authors showed osteoporosis as the most outstanding feature in the microscopic sections. Most of the examined tissue was viable. If vascular damage were the predisposing cause of fractures of the femoral neck, it seems likely that more aseptic necrosis of the femoral head would occur. Significant changes in the blood vessels were not seen in the reported cases. The reparative process following irradiation osteitis is generally retarded because of the extensive damage to the surrounding tissues including the vessels, bone cells and periosteum.

The 12 patients in this report with irradiation damage to the femoral necks represent an incidence of only 0.87 per cent. Four had bilateral fractures. All had received treatment through lateral fields to the pelvis. About 25 per cent of the dose to the pelvis was given through these lateral fields. The average age of the patients was fifty six years. Nine gave no history of trauma. In most cases the first symptom is mild pain in the hip beginning one or two years after irradiation. Limping is a constant sign. Roentgen examination shows a subcapital zone of mottling. A zone of sclerosis may extend across the neck just distal to the head. Separation and displacement may develop or occasionally the neck seems to bend. Irradiation changes are also seen in the pubic bones.

The authors feel that the risk of serious skeletal

damage has been exaggerated and that the use of lateral fields in the treatment of the parametrium should not be abandoned. The incidence of fracture is low and when it does occur the prognosis is usually good.

CLARENCE E. WEAVER, M D

Death from Necrosis of the Bladder, Eight Years After Irradiation for Carcinoma of the Body of the Uterus H Olesen Acta radiol 27 513-516 Aug 31, 1946

While the primary and secondary erythemas of the bladder following irradiation are of slight significance the tertiary reaction is far more serious, leading in some cases to necrosis with fistula formation, and presenting a difficult problem in therapy. The author reports a case of bladder necrosis in a 70 year old woman who eight years earlier had received radium and roentgen therapy for a carcinoma of the body of the uterus. At autopsy no evidence of the uterine tumor was found.

Blood Changes in Radiologic Work. Nils G Norden son Acta radiol 27 416-432 May 6 1946

Material obtained from blood investigations on 1560 individuals working with roentgen rays or radium is presented in comparison with similar studies on 450 individuals not so engaged. Blood changes including leukopenia, granulocytopenia, increased shift to the left, hypersegmentation and pathologic lymphocytes, eosinophilia and basophilia, tendency toward leukocytosis, polycythemia and anemia occurred in 52 per cent of the radiologic personnel. Correlation between the degree of protection and the incidence of blood changes was good when the variation in individual resistance was considered. Significant injuries were observed in about 6 per cent of the group. These the author designates as persistent granulocytopenia and leukopenia combined and pronounced changes in an individual study, hemoglobin of less than 62 per cent, a red cell count of less than three million, a white count of less than 3000 and a lymphocytosis of more than 60 per cent. No serious case of anemia was seen.

ELIZABETH A. CLARK, M D

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Roentgenologic Study of the Small Intestine¹

II Dysfunction Associated with Neurologic Diseases

FRED J HODGES, M D , R WAYNE RUNDLES, M D , and JOSEPH HANELIN, M D

THE GASTRO-INTESTINAL tract is richly supplied with nervous tissue, both intrinsic and extrinsic. The former consists of plexuses beneath the mucosa and between the muscular layers, the latter consists of sympathetic and parasympathetic connections with the central nervous system. Golden and others (2, 5) have suggested that the grossly disturbed function and altered roentgen appearance of the intestine in severe nutritional disorders such as sprue may be due to degeneration of the nerves supplying the gut. Important as the autonomic nerves undoubtedly are in controlling the motor and secretory functions of the gastro-intestinal tract, the clinical manifestations of neurogenic intestinal dysfunction in less exotic diseases certainly are not well established. This may be due to the fact that organic diseases restricted to the autonomic neurons are rare, and that the presenting abnormalities ordinarily relate to disturbed orthostatic blood pressure regulation, defective sweating or thermal regulation, bladder paralysis, etc.

We have approached the problem of investigating the possible role of the autonomic nerves in causing disturbed motor function of the intestinal tract by carrying out roentgen studies in selected patients

TABLE I NEUROLOGIC DIAGNOSES IN PATIENTS SELECTED FOR ROENTGEN STUDY OF THE INTESTINAL TRACT

Diabetic neuropathy	35 cases
Pernicious anemia	20 cases
Tabes dorsalis	5 cases
Miscellaneous neurologic diseases	
Peripheral neuropathy etiology unknown	4 cases
Guillain-Barré syndrome	1 case
Peripheral neuropathy with lead poisoning	1 case
Autonomic nerve paralysis	1 case
Sympathectomy	8 cases

with well defined neurologic disease. Several categories of patients were used (Table I). Since our previous clinical studies (9) have shown that autonomic nerve disease occurs to an unusual extent in patients with diabetic neuropathy and gives rise to strikingly unusual gastro-intestinal symptoms, this group was of particular interest. Intestinal and bladder disturbances are common in the neurologic disease occurring as a manifestation of pernicious anemia, in tabes dorsalis, etc. Other opportunities for investigation occurred in patients in whom the vagus nerves were sectioned in the treatment of intractable peptic ulcer or incidentally during total or subtotal gastric resection. The effect of splanchnicectomy and lower thoracic ganglionectomy was studied in patients in whom this operation was carried out for the treatment of arterial hyper-

¹ From the Departments of Roentgenology and Internal Medicine, University Hospital, University of Michigan, Ann Arbor. Accepted for publication in August 1947.

* Since July 1, 1945 attached to the Department of Medicine, Duke University School of Medicine, Durham, N. C.

TABLE II CLINICAL FINDINGS IN 30 PATIENTS WITH DIABETIC NEUROPATHY AND GASTRO-INTESTINAL SYMPTOMS

Impotence atonic bladder (either or both)	18 cases
Diabetic retinopathy	16 cases
Orthostatic hypotension (drop of 50 mm Hg or more in systolic blood pressure)	8 cases
Hepatomegaly	6 cases
Gastro intestinal symptoms	
Cramps pain borborygmi	22 cases
Anorexia	20 cases
Severe constipation	15 cases
Vomiting	13 cases
Fecal incontinence	8 cases
Diarrhea	7 cases
Alternating diarrhea and constipation	4 cases
Nocturnal diarrhea	3 cases

tension An example of autonomic nerve paralysis occurring spontaneously as a disease entity was also included in the study. It was hoped that investigation of material of this type might contribute to our basic knowledge of neurogenic intestinal dysfunction.

DIABETIC NEUROPATHY

At the outset of the disease individuals afflicted with diabetes mellitus have but one defect, a deficiency of insulin. Under optimal conditions this deficiency can be corrected and health maintained indefinitely. All too frequently, however, imperfect regulation over the course of years permits the development of complications, among which is to be found a characteristic degenerative disease affecting the peripheral nerves. The neurologic disorder resulting from diabetes is a chronic, and often severe, neuropathy with an unusual predilection for the autonomic nerves. This is evidenced by sweating deficiencies, impaired mechanisms of heat regulation, defective orthostatic blood pressure control, neurogenic bladder paralysis, etc. Only when meticulous diabetic regulation is maintained over a period of many months do the neurologic state and the attendant symptoms improve.

✓Gastro-intestinal abnormalities are not found with unusual frequency among patients with uncomplicated diabetes, or even with diabetes which is temporarily out of control. When diabetic neuropathy develops, the majority of patients complain of serious and unusual gastro-intestinal

disturbances. [In a recent study involving a large group of such patients, these abnormalities developed with the neuropathy in over 60 per cent of the cases (9). Symptoms referable to the lower intestinal tract were predominant and usually appeared first. In two-thirds of the cases there was severe and nearly intractable constipation. In the remaining third a chronic diarrhea developed, sometimes alternating with severe constipation and sometimes occurring as a distressing nocturnal diarrhea, often with fecal incontinence.] (11) In those with severe or progressive neuritic disease, symptoms of upper intestinal tract dysfunction were common, including postprandial distention, cramps, profound anorexia, and nausea and vomiting after meals.

Prolonged delay in gastric emptying and disorderly transit of intestinal contents along the intestinal tract were discovered in five of the cases of diabetic neuropathy previously reported (9). Thirty additional diabetics with neuropathy and associated gastro-intestinal symptoms have since been investigated. The diabetic background and neurologic status in this group were comparable to those previously reported. The incidence of associated complications, retinopathy, hepatomegaly, orthostatic hypotension, genito-urinary abnormalities, and gastro-intestinal symptoms is tabulated (Table II). On the basis of appropriate diagnostic procedures, the presence of diseases other than diabetic neuropathy was excluded.

CASE 13 (Fig 9 A 1, 2, 3): G. W., a 29 year-old white farmer, came to the hospital complaining of a painless deformity of the left ankle of two months duration. He had had diabetes since the age of twelve years, but it had always been treated erratically. Five years after the onset, severe diabetic acidosis occurred with the development of a large subcutaneous infection. For five years the patient's general health had been such that he was able to work only about half time. For at least two years his lower legs and feet as well as his forearms and hands had

* Case numbers and figure numbers in this paper follow consecutively those in Part I of this study (Radiology 49:587 November 1947).

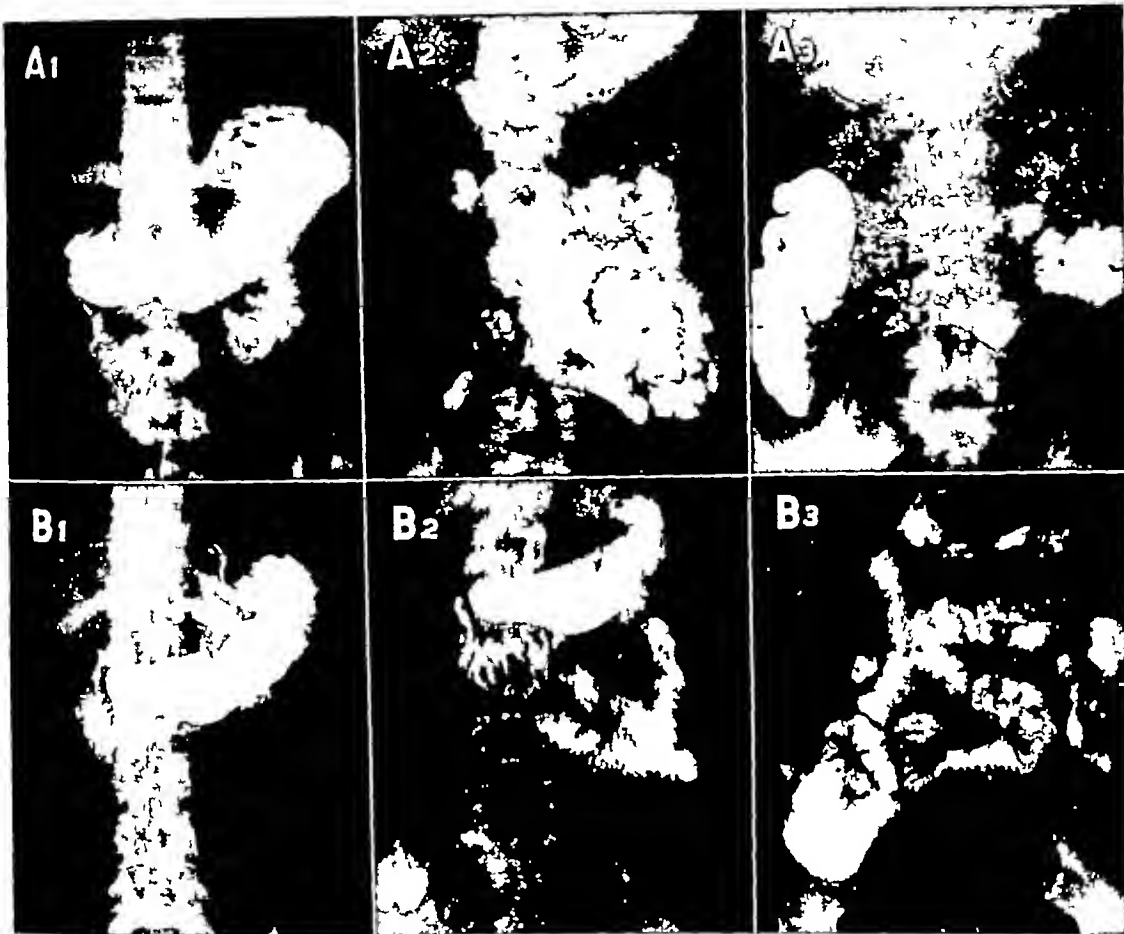


Fig 9 Functional small bowel disturbance

A 1 2 3 Case 13 In this case of poorly controlled diabetes with definite signs of neuropathy exposures immediately, two and a half, and five hours after feeding show delayed gastric emptying prolonged small bowel transit time, considerable variability of small bowel lumen width and displacement of small bowel loops by the distended bladder

B 1, 2, 3 Case 14 Another example of small bowel dysfunction encountered in a patient with diabetes and associated evidences of neuropathy Exposures immediately and at two and a half and five hours again show recognizable signs of dysfunction

felt numb His calf muscles were tender to pressure and became sore after exercise He had noticed the absence of sweating distally in the extremities For four or five years he had spells of diarrhea with six to eight stools per twenty-four hours, most of them occurring at night Two months before hospitalization his left ankle began to swell, lose its normal shape, wobble, and crunch as he walked

On physical examination, the patient appeared to be well developed but weak There were numerous punctate hemorrhages in both optic fundi The knee and ankle reflexes were absent Deep and cutaneous senses were severely impaired below the knees and over the hands There was no sweat secretion or pilomotor function in the lower legs The left ankle was a shapeless joint, the weight being borne on the

head of the fibula The joint was entirely painless to manipulation Serologic tests for syphilis were negative The spinal fluid was normal except for protein content of 160 mg per 100 cc Cystometric examination showed atonic bladder paralysis Roentgen examination of the left ankle joint showed extensive disruption and subluxation of the joint relationships

CASE 14 (Fig 9 B-1, 2, 3) N L L, a 48 year-old married white woman, had had unregulated diabetes for fourteen years, with one bout of diabetic acidosis and a continuous and heavy glycosuria Neuritic symptoms had occurred in the extremities early in the illness For seven to eight years she had suffered from chronic diarrhea occurring especially at night and during the early evening The larger meals were usually

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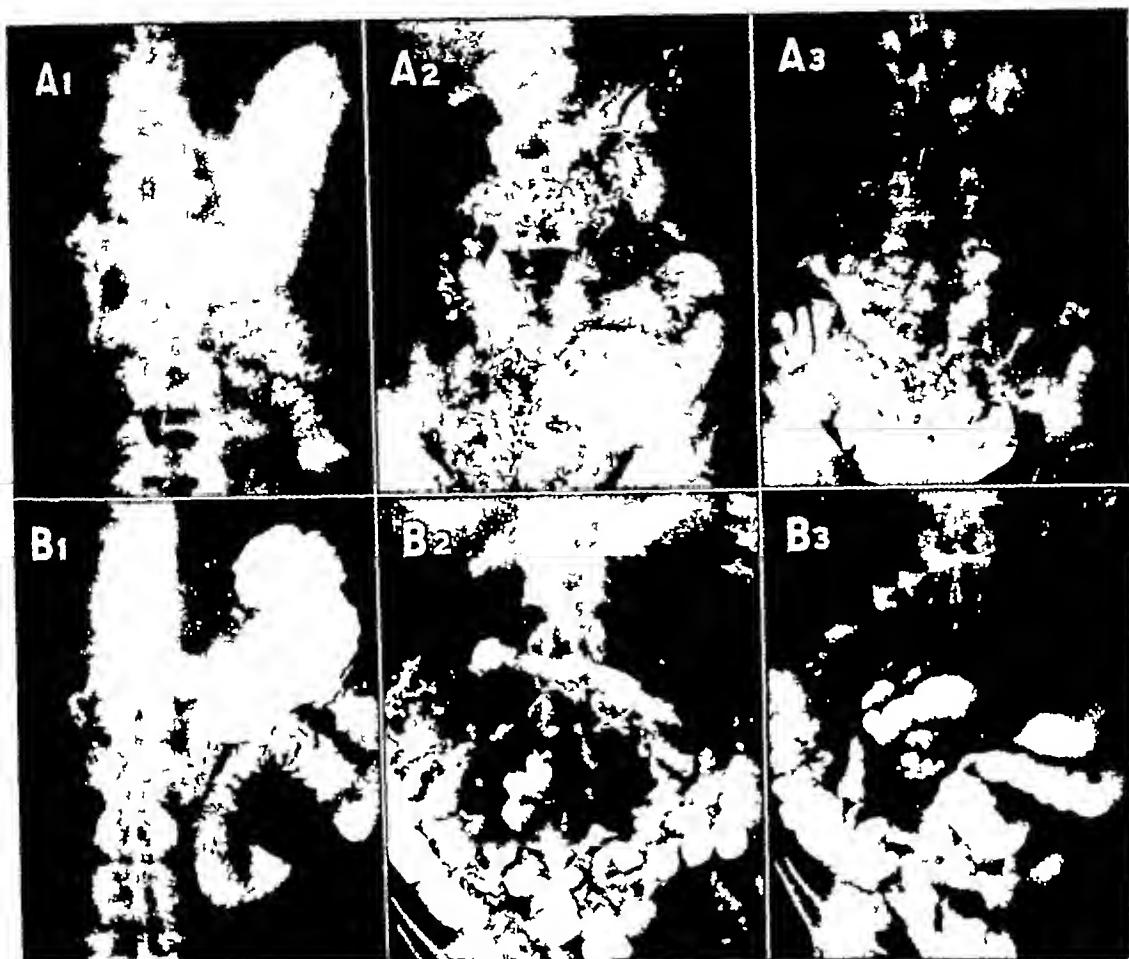


Fig 11 Functional small bowel disturbance

A-1, 2, 3 Case 17 Films made immediately and at two and a half and five hours in another example of diabetes with peripheral neuropathy Delayed transit time is the major feature in this instance

B-1, 2, 3 Case 18 Another example of clear-cut roentgenologic evidence of small bowel dysfunction in a patient with diabetes and peripheral neuropathy Although barium has reached the transverse colon at the five-hour interval, much of the opaque meal has been left in broad and narrow small bowel segments

started, burning pains in the lower legs, severe cutaneous hypersensitivity with desquamation, and finally shallow ulcerations about the toes developed At the time of the neuritic exacerbation a profound anorexia occurred, with a feeling of gastric fullness lasting several hours after eating Gastrointestinal x-ray examination was performed on two different occasions when symptoms were acute After four months of satisfactory diabetic regulation there was definite improvement in the neurologic symptoms Examination showed little evidence of residual neurologic disease All symptoms referable to the gastrointestinal tract had disappeared

CASE 17 (Fig 11 A 1, 2, 3) C E, a 43 year old white truck driver, had had poorly treated diabetes for eight years Heavy glycosuria, loss

of weight, chronic fatigue, impotence, and moderately severe neuritic symptoms developed eight months before hospital admission The symptoms became much worse during a severe upper respiratory infection several weeks later, and at that time the patient's weight fell from 142 to 118 pounds, his appetite vanished, and severe constipation developed Examination in the hospital showed weak, tender muscles in his legs and diminished to absent reflexes At the time of the gastro intestinal examination he complained of poor appetite and severe constipation

CASE 18 (Fig 11 B 1, 2, 3) J F was a 57-year old white salesman Six months before his admission to the hospital he experienced fatigue, lethargy, and severe pain in the legs A heavy glycosuria was discovered, but no treatment was instituted In spite of a large food intake during

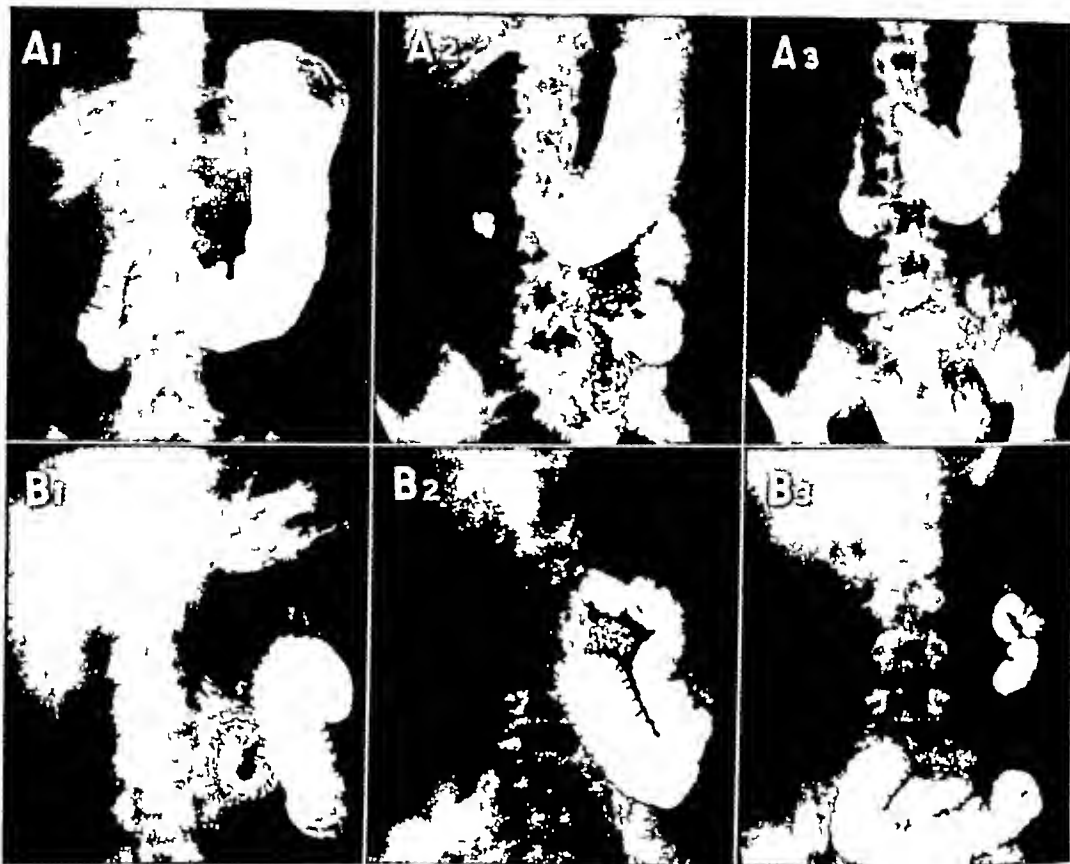


Fig 10 Functional small bowel disturbance

A-1 2 3 Case 15 Exposures immediately and at intervals of two and a half and five hours after feeding in a patient with diabetes associated with peripheral neuropathy. In this instance delayed gastric emptying and delayed small bowel motility are strikingly shown. Note also the very considerable variability of lumen width and the virtual absence of mucosal markings in several bowel loops.

B-1, 2, 3 Case 16 Comparable exposures immediately and at two and a half and five hours in another patient with associated diabetes and peripheral neuropathy. Note here the widened lumen of small bowel and the greatly delayed transit time, as well as considerable amounts of gas within otherwise unfilled loops of small bowel.

followed by cramps, gas, abdominal distention, and urgent bowel movements. Five months before examination, anorexia, frequent vomiting, and fecal incontinence developed.

At the time of physical examination, the patient was obviously chronically ill. The blood pressure in the supine position was 205/100 and on standing 155/80. Bilateral cataracts and diabetic retinopathy were present. Neurologic examination showed severe blunting of the cutaneous senses distally in the extremities. Cystometrie examination showed atonic bladder paralysis.

CASE 15 (Fig 10 A 1, 2, 3) J Q, an 18-year-old white girl, had had diabetes since the age of fourteen. She was not at all cooperative in following any recommended treatment and was in diabetic acidosis several times. Severe diabetic neuropathy finally developed a few weeks

after an episode of diabetic coma. When admitted to the hospital for the treatment of this complication, the patient complained of a complete lack of appetite, nausea with vomiting whenever she ate more than small quantities of food, and periodic diarrhea alternating with severe constipation.

CASE 16 (Fig 10 B 1, 2, 3) M W R, a 17-year-old white boy, had had diabetes since the age of five. His treatment had been erratic and he failed to grow and develop normally. At the age of twelve he developed a convulsive disorder which interfered further with diabetic management. At the time of physical examination he was found to be poorly developed and dwarfed. His liver was definitely enlarged. The tendon reflexes were sluggish or absent.

The patient was admitted to the hospital for diabetic regulation. Four weeks after this was

covered a wide range of abnormality falling under the heading of "disordered motor function" as described by Golden. Some degree of gastric retention, prolonged barium transit through the intestinal tract, and segmentation of the barium column were fairly constant features. The caliber of the gut lumen showed considerable variation, and localized segments of dilated gut were encountered. The mucosal pattern was well preserved in most cases. However, localized coarsening, irregularity, and partial obliteration of folds were not infrequently observed. Scattered gas accumulations in the small bowel were likewise noted in a number of instances.

In many of the patients with diabetic neuropathy, roentgen evidence of disturbed gastro-intestinal function was less conspicuous than the clinical symptomatology would lead one to expect. The deviation from normal, however, was greater among those with severe neuropathy and in those with the more pronounced intestinal symptoms. The type of roentgen abnormality present, with the exception of prolonged gastric retention, gave little clue to the nature of the presenting clinical symptoms in most cases. Abnormalities of the same type and degree occurred in those suffering from severe constipation as in those with chronic diarrhea. Gastric retention and delayed transit through the bowel were found, for instance, in many of those who complained of diarrhea. There were no features by which patients with nocturnal diarrhea could be separated from those with daytime diarrhea. Two patients were re-examined after prolonged treatment had resulted in definite neurologic improvement. In spite of the virtual absence of gastro-intestinal symptoms, the roentgen findings showed that return to normal had been incomplete.

PERNICIOUS ANEMIA

An assortment of gastro-intestinal disturbances has long been included among the classic symptoms of pernicious anemia. With the advantages of modern diagnostic methods and the availability of curative

therapy, these symptoms may now be more precisely analyzed and a group associated with neurologic dysfunction recognized. Mild chronic complaints such as indigestion, limited tolerance for certain foods, post-prandial bloating, the frequent passage of soft stools, etc., are common in uncomplicated cases during complete spontaneous or therapeutic remissions. Profound anorexia with distaste and aversion to food often occurs early in the development of pernicious anemia or during a relapse of the disease before anemia and other clinical manifestations become severe. Renewed appetite and ability to eat follow in two to four days after the beginning of effective treatment. Again, patients who become merely anemic usually suffer from anorexia with vomiting when the hemoglobin level drops below about 5 gm per 100 cc. Alleviation of the symptoms depends upon raising the hemoglobin level by blood transfusion or by effective anti-anemic therapy. None of these symptoms appears to be closely related to the recurrent pain and soreness of the tongue associated with visible lingual abnormalities—lack of coat, atrophy of lingual papillae and, when the anemia is not severe, a scarlet or beefy red color.

A still different train of symptoms is encountered in patients with pernicious anemia who show the more severe degrees of neurologic disorder, especially when this has resulted in neurogenic bladder paralysis, sometimes with the loss of sphincter control (10). Severe constipation, requiring continual catharsis or frequent use of enemas, is the earliest and most persistent symptom. Later abdominal distention, cramps, and borborygmi tend to follow each meal, and in long-untreated cases diarrhea with fecal incontinence develops. These symptoms begin to subside only after several weeks of specific therapy, and improvement parallels restoration of peripheral nerve function.

Among the 20 patients with pernicious anemia in relapse who were available for special small bowel examinations, 10 were simply anemic. Roentgen evidence of

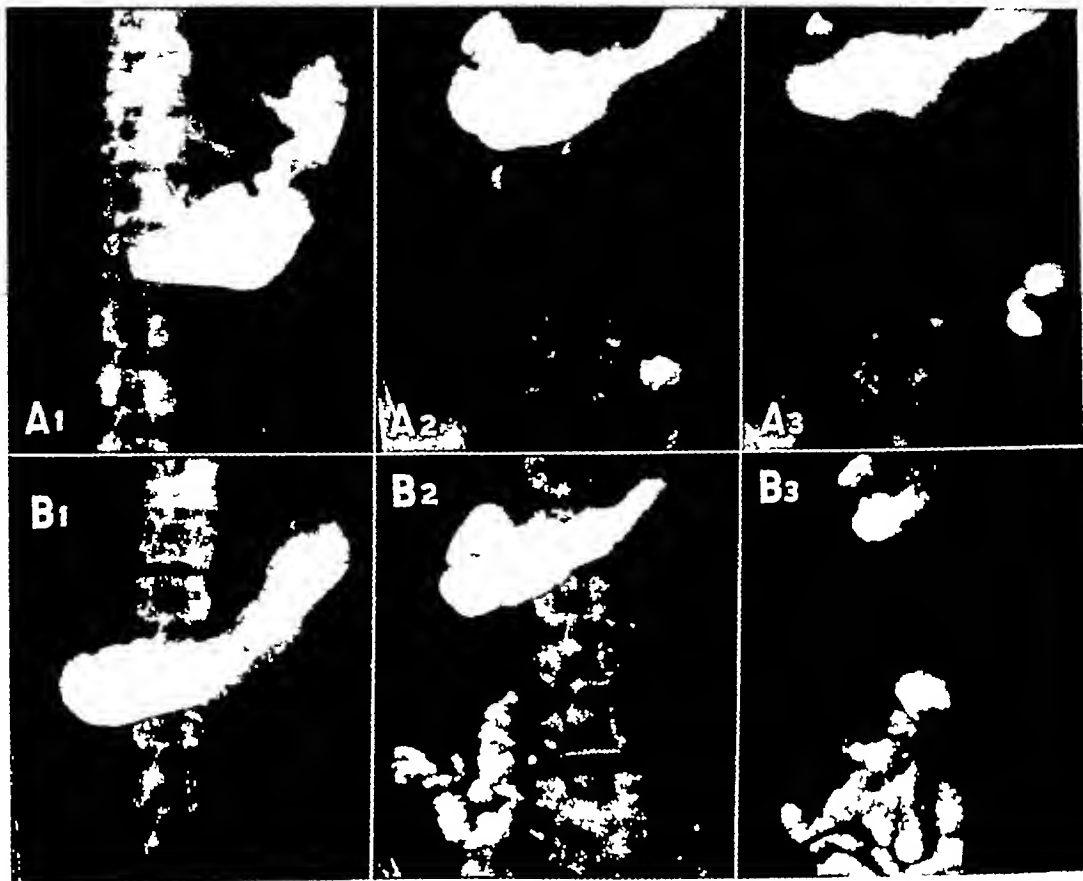


Fig 12 Functional small bowel disturbance

A-1, 2, 3 Case 19 Profoundly delayed gastric emptying as shown in exposures immediately and at two and a half and five hours after feeding in a diabetic with peripheral neuropathy

B-1, 2, 3 Evidence of improved function in same patient following treatment of diabetes

the next few months, his weight fell from the usual 203 pounds to 144 pounds. The pain and weakness in his legs increased until he could not walk. Severe constipation developed, and finally anorexia with nausea after eating. Physical examination disclosed evidence of moderately severe peripheral neuropathy with partial foot drop on the left. During the week preceding the gastro intestinal examination heavy oral and parenteral vitamin B therapy was administered. This form of treatment had no observable effect on the patient's neurologic status and the gastro-intestinal symptoms remained unaltered.

After ten months of careful diabetic regulation the patient had improved generally and was able to walk six or eight blocks without difficulty. The gastro intestinal symptoms had disappeared. Evidence of neurologic disease remained.

CASE 19 (Fig 12 A 1, 2, 3 B 1, 2, 3) E H a 34-year-old white farmer, had diabetes at the age of 20. Following the initial regulation he

abandoned the recommended dietetic regimen and two years later there was an episode of coma. Six years after this he had severe diabetic acidosis and a small lung abscess, which required ten months' treatment in the hospital. His subsequent regulation was aimed only at keeping his urine free of ketone bodies. For six years he had had chronic diarrhea with six to nine stools per day, most of them following meals or at night, when they were accompanied by fecal incontinence.

On entrance to the hospital the patient was fairly well developed and nourished. Blood pressure in the supine position was 200/100 (pulse 114), and on standing 114/80 (pulse 150). Diabetic retinopathy was present. The liver was enlarged. The tendon reflexes were absent and there was severe blunting of the cutaneous senses about the lower extremities. Cystometric examination showed an atonic bladder paralysis.

Roentgenographic findings in these cases

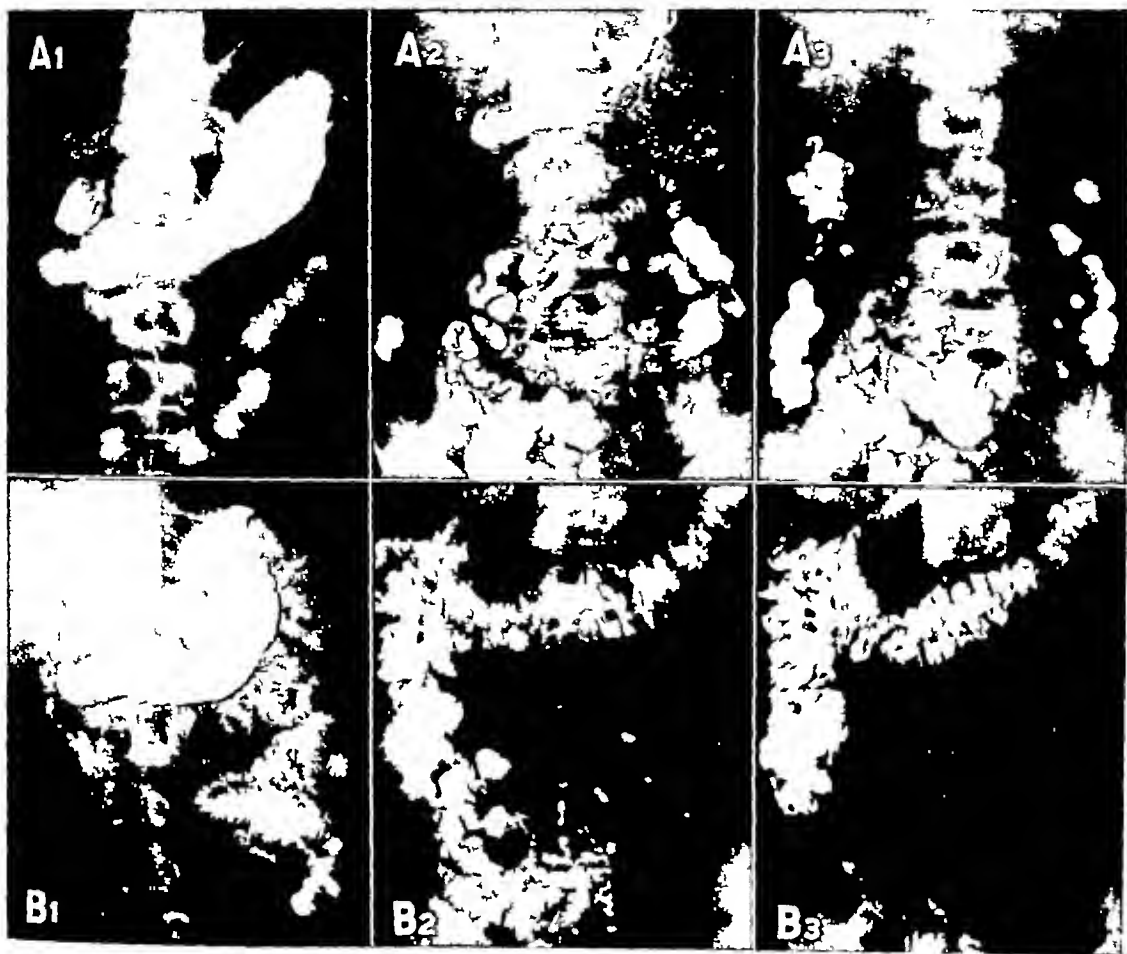


Fig 14 Functional small bowel disturbance

Case 22 The profound and characteristic roentgen signs of small bowel dysfunction shown in films made at once and at two and a half and five hours after feeding (A-1 2 3) have disappeared (B-1 2, 3) in comparable exposures made one year later after the symptoms and signs of pernicious anemia with associated peripheral neuropathy have responded to treatment

pelvis, and cutaneous senses were severely blunted below the knees. Gastric achlorhydria followed histamine injection. There was a severe anemia, with the red blood count reduced to 1,000,000, the white blood count to 2,050, and the hemoglobin to 4.9 gm per 100 cc. The average cell volume was 115 cu microns. Cystometric examination showed an atonic bladder paralysis with an occasional uninhibited contraction.

The patient was treated in the hospital for two months with liver extract injections, with the expected hematologic response. She became more alert and cooperative, and the gastro intestinal complaints, with the exception of persistent constipation and occasional incontinence, disappeared. At the time of discharge she had regained some of her ability to move her legs in bed. After nine months of continued treatment, she was able to walk about, holding to a chair for support. Slight tingling persisted in

her hands and feet. The tendon reflexes in the lower extremities were hyperactive and pyramidal tract signs persisted bilaterally, but there were no sphincter disturbances.

CASE 21 (Fig 13 B-1, 2, 3) A D, a 63-year old housewife, had been treated for pernicious anemia four years before her hospital admission. Regular injections of liver extract had resulted in great improvement for several months, but then treatment was discontinued. For two years the patient had noticed a progressively increasing weakness of the legs, and for one year she could walk only by using a cane. Three months before admission her lower extremities became paralyzed, urinary retention and bowel incontinence developed. Her appetite became extremely poor and there were abdominal distention and occasional vomiting.

On initial examination the patient was found

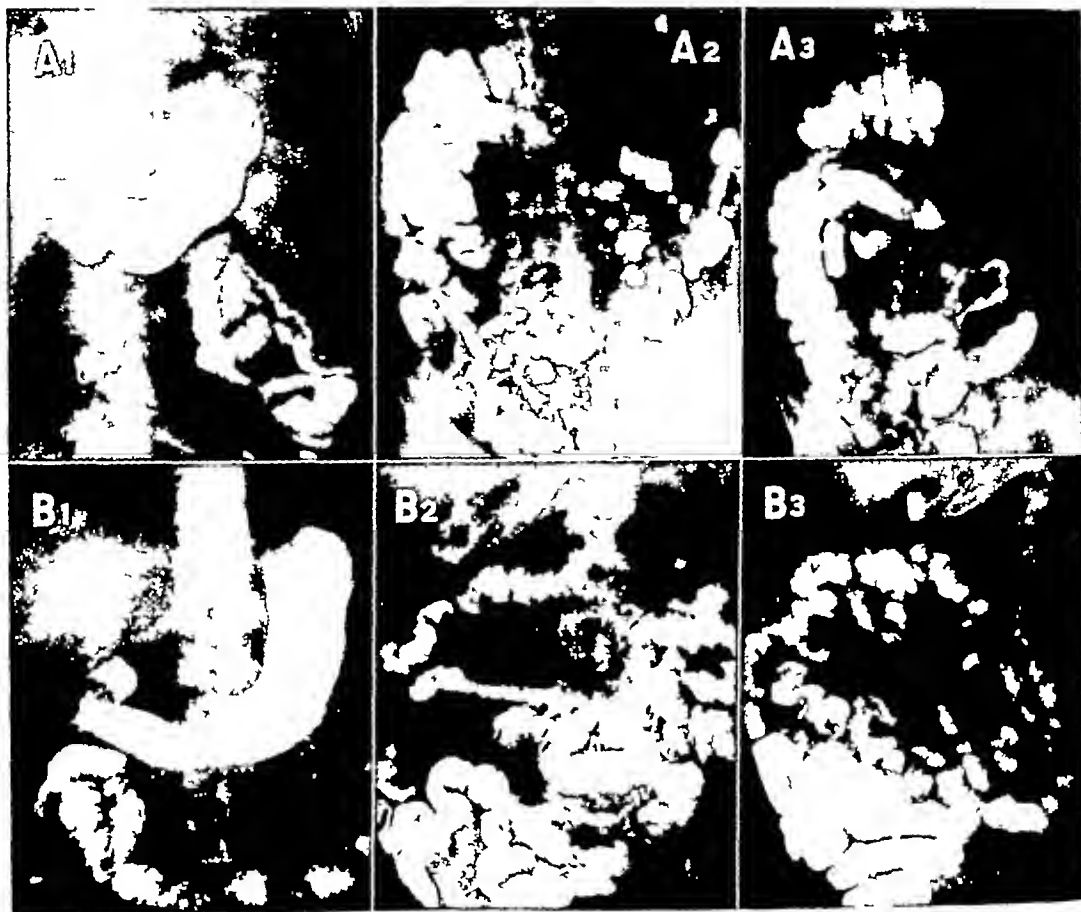


Fig 13 Functional small bowel disturbance

A-1, 2, 3 Case 20 Delayed small bowel transit, segmentation of barium column, and variability of lumen width observed immediately and at two and a half and five hours after feeding in a patient with proved pernicious anemia and associated peripheral neuropathy

B-1, 2, 3 Case 21 Similar though more profound evidences of small bowel dysfunction in another patient with pernicious anemia and peripheral neuropathy. Exposures made immediately and at two and a half and five hours after barium feeding

disturbed intestinal function was unimpressive in this group, and they became symptom free one to four weeks after specific therapy was begun. Five individuals had pronounced atrophy of the lingual mucosa with neither severe anemia nor neurologic disease. Again no definite evidence of intestinal dysfunction was observed. Conspicuous abnormalities were, however, discovered in those patients with severe neurologic disease. Significant gastric retention was not observed, otherwise signs of disturbed intestinal function were not unlike those encountered in diabetics with associated neuropathy. Three illustrative cases are presented.

CASE 20 (Fig 13 A-1, 2, 3) For four to five years, N. R., a 47-year-old white woman, had had a yellowish complexion and poor appetite, with occasional nausea and vomiting. A year previously numbness and tingling in her legs developed. Three months before admission to the hospital she became too weak to walk and could no longer control her legs. Looseness of the bowels with fecal incontinence alternated with severe constipation requiring enemas. Shortly before admission urinary retention occurred.

On examination the patient was found to be mentally confused. She was obese and her skin was lemon yellow in color. Flaccid paralysis of the lower extremities was observed. Knee and ankle reflexes were absent and the plantar responses were upward. Vibratory motion and position senses were impaired to the level of the



Fig 15 Functional small bowel disturbance

Case 23 Greatly delayed transit time after barium feeding in a patient with generalized autonomic paralysis

close at hand were blurred unless he focused on them steadily for some moments. A few days later he began to vomit and have upper abdominal cramps following meals, spells of diarrhea, and finally rather severe constipation. Urinary hesitancy developed, with a weak stream, an uncertain sense of bladder fullness, and complete impotence. Three weeks after the beginning of his illness, the patient began to feel faint when sitting up and would lose consciousness whenever he stood erect. He became confined to bed. Two months after the onset of his illness he was admitted to the University Hospital.

On physical examination, the patient appeared well developed and well nourished. His pupils were about 4 mm in diameter and would not react visibly to light or on accommodation. His tongue was dry. Oral secretions were scant and could not be increased by acid or salt stimulation. In the supine position the blood pressure was 104/60 mm Hg (pulse 72). When sitting up, the patient felt dizzy, his blood pressure dropped to 50/35 (pulse 68) and the radial pulse became weak and difficult to palpate. He was able to stand for only a moment before losing consciousness. Except for the fixed pupils and diminished oral secretions no neurologic abnormalities were demonstrable.

Examination of blood, urine, and spinal fluid showed no abnormalities. Serologic tests for syphilis were negative. Cystometric examination showed atonic bladder paralysis with 300 cc of residual urine. The patient was painted with an iodine mixture dusted with starch, and warmed under bakes until his oral temperature had risen 1.5° F above normal. Slight sweating was produced about his face and neck, but elsewhere it was nearly absent.

X-ray examination on two different occasions

showed a large, sluggish stomach with retained food and secretions. The caliber of the intestinal loops was somewhat increased, and transit along the tract was markedly delayed, so that at five hours the head of the barium meal had not progressed beyond the proximal jejunum.

The patient was treated symptomatically with ephedrine, amphetamine, and increased salt intake. When out of bed, he wore rubber stockings and a snug corset. After eight weeks in the hospital, he was able to be up and around much of the time. At home he improved gradually until he could resume farm work. Eleven months after the beginning of his illness his symptoms had largely disappeared and he reported that his family physician found his blood pressure well maintained when standing.

EXTRINSIC DENERVATION OF THE GUT

Abundant evidence has been presented above to show that neurologic disease affecting the autonomic nerves is productive of gastro-intestinal symptoms and convincing roentgen evidence of abnormal function. The problem next arises as to whether the responsible neurologic disease involves the extrinsic, sympathetic and parasympathetic neurons, or the intrinsic plexuses, or both. Information bearing on this point has been gained by studying patients in whom the vagus nerves have been resected in the treatment of intractable peptic ulceration, and in patients subjected to sympathectomy in the treatment of arterial hypertension.

to be confused and apathetic. The appearance of her tongue was normal. There was a flaccid paralysis of the lower extremities. The knee and ankle reflexes were absent, the plantar responses doubtful. There was severe blunting of the cutaneous senses below the knees. A macrocytic anemia was present, with reduction of hemoglobin to 8 gm per 100 cc. A cystometric examination showed an atonic bladder paralysis.

After six weeks of treatment with liver extract, the blood values were approaching normal. The appetite was fairly good and the patient was eating well. There was slight abdominal pain associated with gaseous distention and recurrent fecal incontinence.

CASE 22 (Fig 14 A-1, 2, 3, B-1, 2, 3) A summary of the findings in this case has been reported previously (10). F B, a 44-year-old male, had been well until one year before admission to the hospital, when numbness and tingling appeared in his fingers. Six or eight months before admission paresthesia developed in his lower extremities, finally ascending as high as his waist. At times his tongue was sore and noticeably red. He suffered from severe constipation and lost his appetite. Two months before admission to the hospital he began to stagger when walking and for two to three weeks had been unable to walk without support.

On physical examination the patient was found to be well developed and nourished, but was unable to walk without assistance. The vibratory, motion, and position senses and the cutaneous senses were blunted peripherally over the extremities, and extensor plantar responses were present. There was complete atrophy of the lingual papillae. Anemia with reduction in the hemoglobin to 7.9 gm per 100 cc was present. There was gastric achlorhydria following histamine injection.

After the institution of liver extract therapy, the patient rapidly became better and all manifestations of the disease subsided. Five months after the initial examination he was back at work full time. One year after treatment was started, he had no significant neurologic complaints or residual evidence of disease. The gastro intestinal complaints had subsided.

TABES DORSALIS

Not infrequently gastro-intestinal disturbances are a major complication where syphilitic infection of the nervous system has led to tabes dorsalis. The dorsal root ganglia of the cerebrospinal nerves are generally regarded as the chief site of neurologic involvement. While bladder

paralyses in tabes have been extensively investigated, the intestinal abnormalities have received less attention. Five of our patients with tabes dorsalis due to syphilis were of special interest from the roentgenologic standpoint. Three of them were subject to "gastric crises"—acute episodes of upper abdominal pain with nausea and vomiting, lasting from two to ten days before subsiding abruptly. Only one had definite evidence of intestinal dysfunction, as indicated by prolonged barium transit time. Examinations during a period of persistent nausea and vomiting and during a symptom-free period showed no essential differences. Another patient had persistent constipation alternating with loose stools. A fifth patient was incapacitated by abdominal distention following meals, noisy intestinal peristalsis, diarrhea, urinary and fecal incontinence. Roentgen evidence of intestinal disturbance was unimpressive in these cases.

MISCELLANEOUS NEUROLOGIC DISEASES

Roentgen evidence of intestinal dysfunction was inconstantly found in patients suffering from the common types of peripheral nerve disease. Definite alteration in gut caliber and transit time, however, were observed in one patient with the Guillain-Barré syndrome complicated by bladder paralysis and in another patient with severe lead poisoning. Roentgen abnormalities observed in these cases seemed to parallel the degree of coincident autonomic nerve disease. A unique opportunity to examine the gastro-intestinal tract when a naturally occurring disease had resulted in generalized autonomic nerve paralysis was presented by the following case.

CASE 23 (Fig 15 A, B, C) A F, a 42 year-old farmer, had always enjoyed good general health. Two months before the onset of his acute illness he had an upper respiratory infection with malaise and fever, from which he recovered slowly. In the middle of February 1944, his mouth and throat became persistently dry, and solid food began to stick in his throat. He suffered from excessive perspiration and fever. He was able to see distant objects well, but those

Figure 16 A-1 is a reproduction of a film made after barium feeding, showing a duodenal ulcer deformity, active gastric peristalsis, and delicate mucosal pattern of the upper small bowel. After vagotomy (Fig 16 A-2, 3), in the same patient, the stomach is dilated, gastric emptying is delayed, and passage of the barium along the intestinal tract is slower. Distention of the stomach together with prolonged retention and sluggish peristalsis were found to be characteristic features following vagotomy in a large patient group. In association with the above findings, slight increase in jejunal caliber, coarsening of mucosal pattern, and delayed transit time were commonly encountered (3).

An expected postoperative complication following resection of the splanchnic nerves and lower thoracic sympathetic ganglia is a train of symptoms referable to the upper gastro-intestinal tract. For some weeks after the operation most patients have a complete absence of hunger and a profoundly diminished appetite for food. Nausea and vomiting may follow overfeeding. Intestinal cramps and pain, easily distinguished from the radicular pain following resection or traumatization of intercostal nerves, are often severe. Abdominal distention, tenderness to deep palpation, and increased peristaltic activity are commonly present. The disturbances subside in a few weeks and do not reappear.

Roentgen examination of the bowel was performed before and after operation in eight patients in whom it was necessary to treat arterial hypertension by bilateral supradiaphragmatic splanchnicectomy and lower dorsal sympathetic ganglionectomy. Before the operation, these patients had had no significant gastro-intestinal symptoms. After the operation, however, symptoms as described above occurred. Postoperative x-ray examinations were made ten days to four weeks after opera-

tion, when the patients had been out of bed and walking to the bathroom as they pleased for several days. Figure 16 B-1, 2, 3 shows the normal appearance of the stomach and small bowel in a patient with hypertension. Figure 16 C-1, 2, 3 shows comparable exposures in the same patient obtained two weeks following operation. In this instance, the alteration in appearance and behavior of the stomach and small bowel is striking. The majority showed nothing more than delayed transit time following the operation. In other patients, in whom more extensive sympathectomies were done, with removal of the entire sympathetic chains from the first thoracic to the second lumbar ganglia, in two stages, no more dramatic changes were observed. Subsequent examinations as late as three months after operation showed very little or no deviation from the normal except slight slowing of transit time (1).

DISCUSSION

Despite the increasing literature in recent years concerning small intestine disorders, accurate clinical recognition of such disturbances in day-by-day practice is still uncommon. Unless severe nutritional deficiencies or actual intestinal obstruction develop, typical symptoms are apt to be dismissed as being "non-characteristic," "functional," or "psychogenic" in origin. Such symptoms, of course, are characteristically random, changeable complaints associated with other evidences of emotional instability, and remain perpetually benign without leading to serious physical consequences. No convincing evidence has been presented to show that emotional turmoil or psychiatric disturbances alone are capable of consistently altering the expected roentgen appearance of the intestinal tract. In the ordinary process of diagnosis, common lesions of the stomach, duodenum, and colon should be excluded at

B 1, 2, 3 Normal appearance of stomach and small bowel immediately and two and a half and five hours after feeding in a patient with hypertension.

C 1, 2, 3 Comparable exposures in the same patient obtained two months later, following bilateral supradiaphragmatic splanchnicectomy. The alteration in appearance and behavior of the stomach and small bowel as the result of splanchnic interruption is striking in this instance.

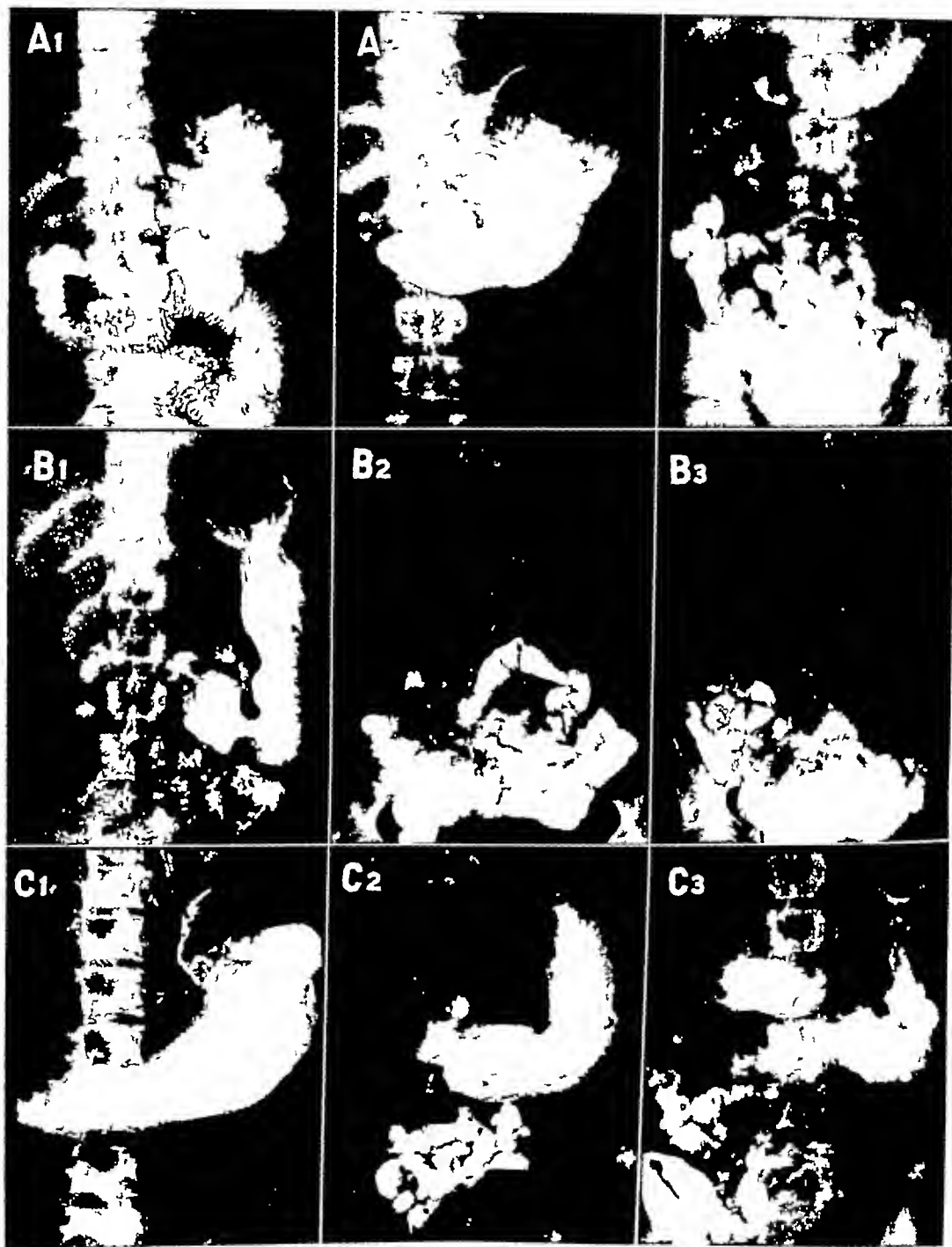


Fig 16 Functional small bowel disturbance following surgical procedures

A 1 Upper gastro intestinal tract immediately after barium feeding showing deformity of duodenal ulcer. Note multiplicity of peristaltic contractions and delicate mucosal pattern of upper small bowel.

A-2 3 Exposures made immediately and five hours after feeding in the same case following vagotomy for relief of ulcer symptoms. Note altered appearance of the stomach, delayed gastric emptying, delayed small bowel motility, despite advance of some opaque material into the transverse colon. In this instance alteration of stomach and small bowel behavior has followed the purposeful interruption of autonomic nerve supply.

[Legend continued on opposite page]

patients with primary dietary deficiencies studied in our series, including an instance of severe pellagra of nearly thirty years' duration, roentgen evidence of small bowel disturbance was not impressive in comparison with the other types of cases cited.

Chronic inflammation of the small intestines certainly occurs oftener than is positively diagnosed. Little is known of the natural history of the non-stenosing types of ileitis and ileojejunitis. The recent production of a chronic inflammation simulating regional ileitis by the injection of homologous serum is of extreme interest (7). Although disturbed nutrition is commonly observed in inflammatory diseases of the intestine, the structural and motor abnormalities frequently persist to a lesser or greater extent after their correction. No specific therapy is as yet effective in eliminating the infection, and surgical removal of the diseased segments of the gut is often eventually necessary.

Evidence has been presented that autonomic nerve disease occurring as an isolated disorder, or as one aspect of a more extensive neuropathy, may produce grave disturbances in gastro-intestinal function. Most naturally occurring neuropathies probably affect both the extrinsic and intrinsic neurons. The relative importance of each is difficult to estimate in individual cases. The extrinsic sympathetic innervation of the gut appears to be of minor importance in controlling motor function, since in most cases little alteration follows operative resection. Surgical removal of the parasympathetic innervation of the upper gastro-intestinal tract by vagus nerve resection results, however, in marked alteration in both motor and secretory function (1). The tendency toward more frequent, softer stools, or even severe

chronic diarrhea, which follows vagotomy in a considerable percentage of cases is noteworthy. The parasympathetic autonomic nerves appear to be of generally greater importance in influencing intestinal function than the sympathetic. Preliminary observations indicate, also, that in the treatment of neurogenic intestinal disturbances the long-acting parasympatheticomimetic drugs are of definite promise.

Department of Roentgenology
University Hospital
University of Michigan
Ann Arbor, Mich

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Spanish summary on following page

the outset, as such organic diseases may disrupt the function of the whole tract. Rare complications should not be overlooked, such as gastrocolic fistulae or any side-tracking operation, as these may produce striking nutritional disturbances and intestinal abnormalities (4). As one's familiarity with the distinctive symptoms of small bowel dysfunction increases, however, initial recognition of the situation becomes possible.

The commonest symptom indicating the need for roentgen examination of the small bowel is any gross change in bowel habit, such as intractable constipation with alternating diarrhea or chronic diarrhea in the absence of organic colonic disease. Another indication is localized or diffuse colicky abdominal pain associated with increased intestinal peristalsis, borborygmi, and gaseous distention. Occasionally small bowel dysfunction will result in greatly delayed gastric emptying in spite of free passage of barium into the upper intestinal loops. We have observed well marked intestinal dysfunction in two patients who were typical examples of the clinical syndrome "anorexia nervosa." A further indication is unexplained bleeding from the intestine, gross or occult, or recurrent anemia, which is particularly suggestive of chronic inflammatory disease or neoplasm of the small bowel.

A confirmed diagnosis of small intestine disease is practically dependent in most cases upon roentgenologic study. The limitations of standard routine procedures in this regard should be clearly appreciated, as well as the fact that many patients with genuine disturbances will not have conspicuous roentgen abnormalities even when the intestine is adequately studied. While errors in roentgenologic interpretation can easily be made in considering minor deviations as reliable evidence of disease without regard to the range and variability of the normal, consideration of all the facts bearing on the case will usually lead to a reasonable conclusion.

When convincing abnormalities of the intestine are uncovered, the findings will

frequently fail to justify a positive diagnosis as to etiology. Localized abnormality of the small intestine may exhibit features which are fairly characteristic of inflammatory or neoplastic disease (3). However, it must be borne in mind that widespread evidence of intestinal dysfunction may occur in the presence of organic disease, and the local lesion itself may be entirely obscured by these changes. While this occurs more often with segmental or regional enteritis, neoplastic involvement of gut, either localized or generalized, may result in a similar appearance. A great variety of conditions may lead to intestinal dysfunction beside the above, among which are primary and secondary nutritional diseases, intestinal parasitism, hypoproteinemia, autonomic nerve disease, neuromuscular degeneration, purpura, etc. In most instances, therefore, the roentgenologist must content himself with a report of "intestinal dysfunction" and await appropriate clinical study, with specific therapy when available, and follow-up examinations to settle the diagnosis. Effective therapy is unlikely in the absence of a correct diagnosis.

The widespread use of "deficiency pattern" as an inclusive term suggesting roentgenologic evidence of disease essentially due to lack of common vitamin fractions in the diet may easily lead to serious misinterpretation. There is no confirmation of the idea that simple nutritional deficiency is the common denominator in diverse intestinal diseases. Early observers were undoubtedly correct in emphasizing the non-specific nature of the described changes (5, 6, 12, 13). It is unsafe to regard structural abnormalities in the gut as representing primary nutritional deficiencies beyond the extent to which they can be corrected in a few weeks' time by specific therapy, as can other deficiency manifestations. It has been shown experimentally that nutritional inadequacy may, however, predispose to secondary inflammatory changes (8), and evidences of the latter may persist in spite of nutritional rehabilitation. In the small number of

Newer Methods of Pneumoarthrography of the Knee with an Evaluation of the Procedure in 315 Operated Cases¹

ISADORE MESCHAN, M.D

Professor of Radiology, University of Arkansas School of Medicine, Little Rock, Ark.

and

W H McGAW, M D

Department of Orthopedics, University Hospitals, Cleveland, Ohio

INTRODUCTION

THE EARLIEST recorded use of pneumoarthrography of the knee was made by Werndorff and Robinson (1) in 1904, and although numerous studies of the method have been made since that time, it has not achieved widespread popularity as a diagnostic procedure, for several reasons

In the first place, the method requires extensive experience so that a good technic may be developed and film studies can be accurately interpreted. Most reported series of cases in this country have been small, and the accumulated experience of any one man has been limited.

In the second place, there has been some misunderstanding regarding the inherent danger of the method. Kleinberg (2) has reported the occurrence of air embolus, but in that instance adequate precautions were not taken to make certain that the needle was not in a blood vessel. Actually, this danger is inherent in any subcutaneous or intramuscular injection if such precautions are neglected. In over 800 pneumoarthrographic studies we have had not a single complication, nor were any complications encountered in Oberholzer's series of 1,200 cases (3). Hauch (4) has cited a personal communication from Samuel in which infection was mentioned as a complication. This danger is certainly minimal if proper surgical asepsis is employed. We have had no case of sepsis in our experience. If pneumoarthrography is attempted in the presence of joint effusion, the effusion may be temporarily increased. Since we have found,

however, that the occurrence of fluid diminishes the efficacy of the method, we refrain from employing it in the presence of joint effusions so far as feasible.

Finally, the value of the method has not been accurately assayed in many large series of cases. There are numerous reports in the German literature, but, as pointed out above, most of the reported series from this country are small. Kleinberg (5), in 1921, reported a small series but was not overly successful at that time. He recommended the method for detection of loose bodies and hypertrophied synovial tissue, but not for detection of loose or injured semilunar cartilages. Bernstein and Arens (6) injected carbon dioxide into the knee joint and likewise showed the usefulness of the method for the diagnosis of synovitis but not for semilunar cartilage abnormalities. Rechtman (7) emphasized the value of pneumoarthrography as affording an opportunity for a definite pathologic diagnosis instead of the somewhat vague "internal derangement." Operative procedures could thus be accurately planned instead of being merely exploratory.

Bircher (8) reported 250 cases in which 3 to 5 c c of abrodil (20 per cent) were combined with oxygen for contrast, giving good diagnostic results. The use of lipiodol in the knee is contraindicated by the study of Burman, Tunick, and Pomeranz (9). Boyd (10) used iopax in a small number of cases, but largely for demonstration of the bursae rather than the semilunar cartilages, and quantities of less than 60 c c were recommended because of the possibility of irritation.

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SUMARIO

Estudio Roentgenológico del Intestino Delgado

II Disfunción Asociada a Neuropatías

Tratando de determinar el posible papel que corresponde a los nervios del sistema autónomo en la etiología de la disfunción motriz del tracto intestinal, efectuáronse estudios roentgenológicos en enfermos que mostraban bien definidos trastornos neurológicos, incluso neuropatía diabética, anemia perniciosa con disfunción neurológica, tabes dorsal y un caso de parálisis neuroautónoma que sobrevino espontáneamente como entidad patológica.

Obtuvieronse pruebas de que una neuropatía del parasimpático, ya se presente como trastorno aislado o como aspecto de una neuropatía más difusa, puede ocasionar graves perturbaciones de la función gastrointestinal, que pueden ser observadas clínica y radiográficamente. Los hallazgos roentgenológicos abarcaron una amplia escala de anomalías encasilladas en el encabezado general de "disfunción motriz" del tubo digestivo.

A fin de determinar el relativo papel de las neuronas extrínsecas, simpáticas y parasimpáticas y de los plexos intrínsecos en la producción de tales trastornos, ejecutáronse investigaciones roentgenológicas en enfermos en quienes se había verificado una vagotomía por úlcera péptica o fortuitamente durante una resección gástrica y en otros que habían sido objeto de una esplenocetomía y ganglionectomía torácica baja por hipertensión arterial. La innervación simpática extrínseca pareció revestir importancia secundaria en la regulación de la función motriz del intestino, dado que en la mayor parte de los casos se observó poca alteración consecutivamente a una resección. En cambio, la extirpación cruenta de la innervación parasimpática de la porción superior del aparato gastrointestinal por medio de la vagotomía produjo marcada alteración en la función tanto motriz como secretoria.



clinical and pneumoarthrographic errors in 101 operated cases among 207 studied by pneumoarthrography and found the method of considerable aid. Five hundred and eight pneumoarthrograms had been done by the time their paper was published, but only the first 207 of these were statistically analyzed (101 operated cases).

The present series of 315 operated cases (including the series reported by McGaw and Weckesser) from an overseas Army General Hospital is reported so that an accurate assay of the method can be made on the basis of a large material. Since an extensive experience with this method is necessary for interpretation of film findings, it has been deemed advisable to illustrate many different types of abnormalities as well as the wide limits of normal, in the hope that the procedure may be more widely and effectively employed.

ANATOMICAL CONSIDERATIONS

The *medial semilunar cartilage (meniscus)* is larger than the lateral, and its cornua are widely separated (Fig 1). It is attached anteriorly to the transverse ligament, the anterior base of the anterior crucial ligament and the non-articular surface of the tibia. Posteriorly, its attachment is to the posterior intercondylar fossa of the tibia in front of the posterior crucial ligament. The circumference of the cartilage is attached to the synovial and fibrous capsules of the knee joint and the internal collateral ligament. The superior and inferior surfaces of the meniscus are not attached to any structures in the knee. The anterior cornu does not lie entirely on the rim of the tibia, as it is attached to the transverse ligament.

The *lateral semilunar cartilage (meniscus)* lies entirely on the rim of the lateral tibial plateau and has no peripheral capsular attachment where the popliteus muscle crosses it, here the cartilage is covered by synovial membrane. This meniscus is smaller in diameter, thicker about the periphery, and usually wider than the medial. It is attached posterior to the base of the anterior crucial ligament (unlike the me-

dial) and anterior to the posterior crucial ligament near the intercondylar fossa.

Both menisci are covered with synovial membrane except at the rims of attachment. They are triangular in cross section. Microscopically, they contain a core of fibrous tissue arranged transversely and longitudinally, with a covering above and below of white fibrocartilage.

The *infrapatellar fat pad* is extrasynovial and is attached by a fold of synovial membrane (ligamentum mucosum) to the intercondylar portion of the femur (Fig 4, C). The alar folds are found on either side of the ligamentum mucosum.

The *suprapatellar bursa* is lined by synovia and communicates with the joint space and with the posterior capsule. The latter consists of two globular-like bursa structures on the posterior aspect of the femoral condyles (Fig 4, C).

The *posterior capsule* may in turn communicate with another out-pouching called either a popliteal bursa or cyst (22) (Baker's cyst) (Fig 33).

TECHNIC

Method of Oxygen Insufflation. Oxygen is recommended for pneumoarthrography because it is quickly absorbed from the knee joint and is non-irritating. Eighty to 120 c.c. of oxygen are injected under gentle pressure into the joint space after the usual antiseptic preparation of the field and local infiltration of 2 per cent procaine down to the joint capsule. Surgical aseptic technic is employed (Fig 2, A and B). The injection is made on the lateral aspect of the knee just below the junction of the quadriceps tendon with the superior articular margin of the patella (Fig 2, B). The patella is displaced laterally to facilitate the insertion of the needle. As the needle passes through the capsule an initial resistance may be encountered, but if the needle is in proper position, after the first few cubic centimeters the injection proceeds easily. Usually the patient can tell the operator that the oxygen is entering the joint. The operator, on the other hand, can usually feel and see the swelling of the

Forced abduction or widening of the joint space has been used by a number of investigators. Dittmar (11) used this procedure in children or adults where there was weakness of the collateral ligaments. Felsenreich (12) showed subluxation of the medial meniscus by forced abduction but considered the method rarely of value here, though useful in testing the integrity of collateral ligaments. Nordheim (13) and also Evans (14) showed that forced abduction or traction leaves a vacuum providing contrast for the shadow of the semilunar cartilage, but after a number of minutes, fluid replaces the vacuum and contrast is no longer obtained. This was found to

irritant effect. Negative contrast studies he found of definite value.

Cullen and Chance (18) were apparently the first to report pneumoarthrographic studies employing a horizontal x-ray beam in anteroposterior projections of the knee. In a series of 22 explored patients, they found definite lesions in 18. We have modified their method by placing the knee on a fulcrum so that the weight of the leg spreads the uppermost part of the joint space where the gas accumulates.

Somerville (19) recently (July 1946) supplemented a previous preliminary report (1943) with an analysis of 331 knee examinations by air arthrography. He

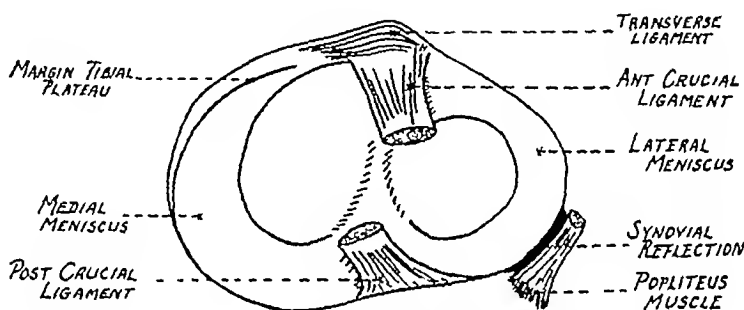


Fig 1 Top view of tibial plateau. Note especially the synovial reflection over the popliteus muscle.

be true for about 70 per cent of cases in Evans' series with regard to the medial meniscus, and for some 6 per cent with regard to the lateral meniscus. In the presence of fluid, Nordheim injected air into the joint space as an aid to diagnosis, being thus the first to employ a combination of forced abduction or traction and air contrast in the knee.

Simon, Hamilton, and Farrington (15) reported a series of 21 cases of traumatic knee injuries examined with the aid of air injection, from which 28 cartilages were removed. Quaintance (16) published a series of 50 operated cases and recommended pneumoarthrography as valuable.

Hamilton (17), in 1939, reported on the use of both opaque and non-opaque media in knee pneumoarthrography and concluded that the use of a positive contrast fluid is not warranted in view of its possible

employed a curved cassette and oblique views of the menisci. He also opened the partially flexed joint by forcible abduction or adduction and applied a firm bandage above the knee. Two hundred and thirty-seven cases came to operation. In 211 (89 per cent) the arthrogram was proved to be correct. In 16 cases among 21, prediction of a negative finding was correct, and in 195 cases out of 216 the lesion subsequently found in the knee was accurately diagnosed.

Recently, Blonek and Wolf (20) and Hauch (4) have reviewed this subject. Blonek and Wolf used 3 to 5 c.c. of 35 per cent hippuran and 150 to 200 c.c. of oxygen. Hauch used only oxygen, to the point of discomfort. Many types of internal derangement were recognized, but both series were small.

McGaw and Weckesser (21) evaluated

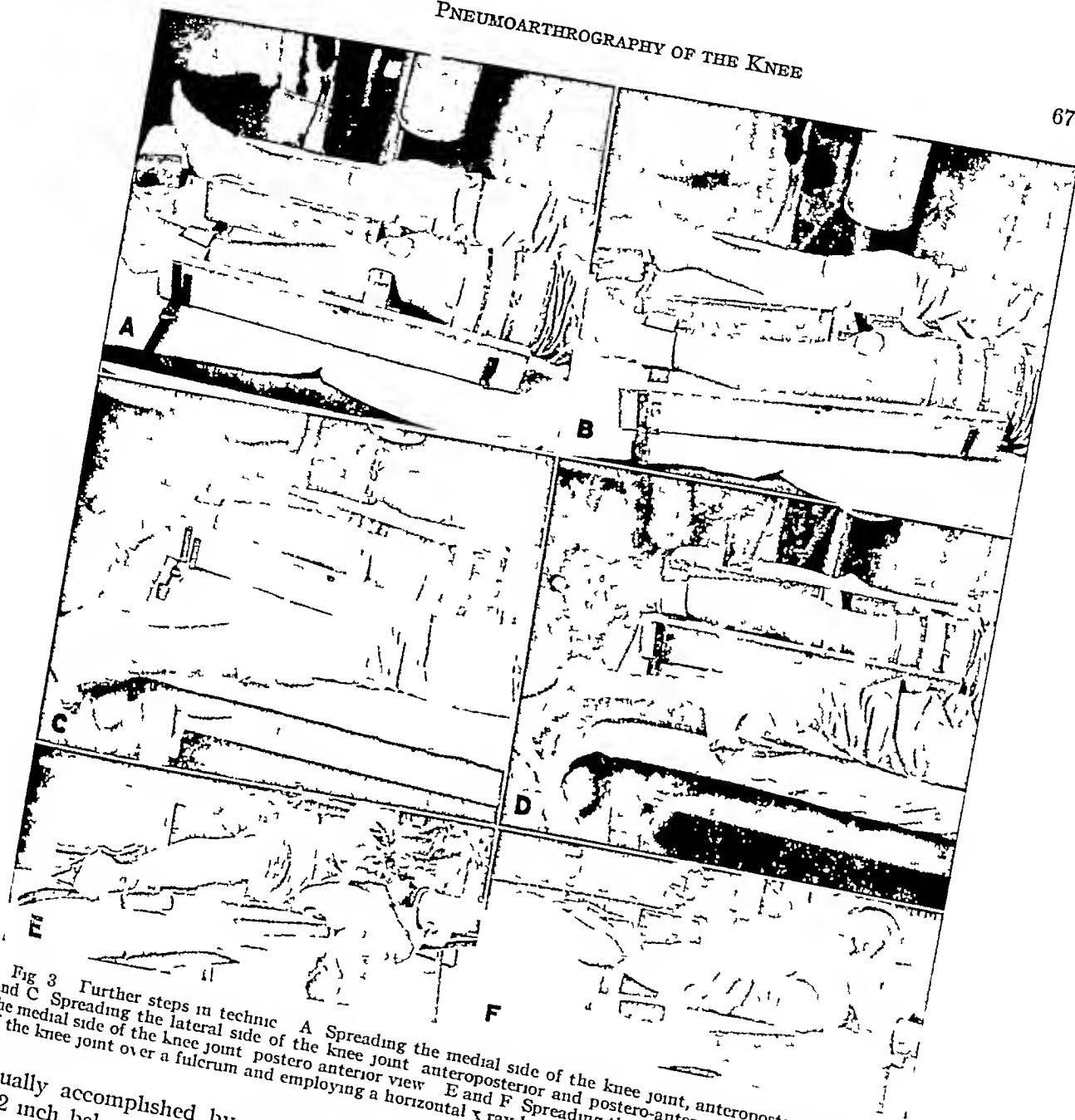


Fig 3 Further steps in technic A Spreading the medial side of the knee joint, anteroposterior view B Spreading the lateral side of the knee joint, anteroposterior and postero-anterior views C Spreading the medial side of the knee joint, postero-anterior view D Spreading the lateral side of the knee joint, postero-anterior views E and F Spreading the lateral (E) and medial (F) sides of the knee joint over a fulcrum and employing a horizontal x ray beam

usually accomplished by centering about 1/2 inch below the inferior tip of the patella, or by palpating and marking the upper margin of the tibia. An alternate method is to mark the patient under fluoroscopic control.

The following views are routine (1) anteroposterior, spreading the medial side of the joint with block pressure laterally (Fig 3, A), (2) anteroposterior, spreading the lateral side of the joint with pres-

sure medially (Fig 3, B), (3) postero-anterior, spreading the medial side of the joint space with pressure laterally (Fig 3, C), (4) postero-anterior, spreading the lateral side of the joint space with pressure medially (Fig 3, D), (5) a straight lateral view with the knee partially flexed.

The usual factors employed are, for the anteroposterior and postero-anterior views, 55 kv p, 15 ma, 0.25 second, 30 inch distance, par-speed screens, small focus, for

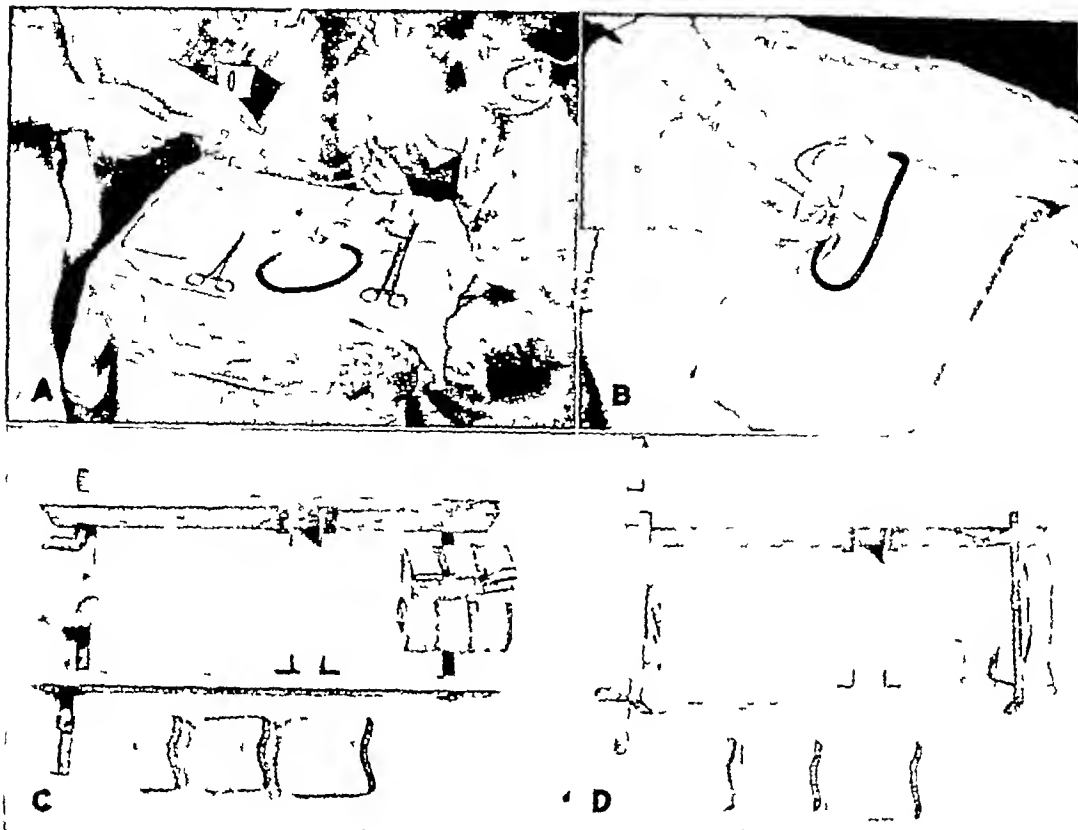


Fig 2 Steps in the technic of oxygen injection and radiography A The adapter for loading the syringe with oxygen is handed to the assistant for connection with the oxygen tank B The skin is prepared as for any surgical procedure and the knee is draped The patella is pushed laterally as the needle is inserted near its superior articular margin C and D Knee spreading device viewed from above (C) and below (D)

suprapatellar bursa The injection is continued to the point of initial discomfort and slight positive pressure in the joint The needle is quickly withdrawn and finger pressure is applied over the point of entry for several minutes to seal the opening in the bursa Gentle massage and movement of the knee will facilitate the circulation of the oxygen through the joint

Method of X-ray Examination In order to distribute the air in the joint, and to prevent its loculation in the suprapatellar bursa, the patient is turned into the prone position and the knee is massaged and flexed several times The patient is then transported to the x-ray examining table

Evans (14) has indicated that spreading the medial joint space allows visualization of the semilunar cartilages in about 70 per cent of cases even without contrast ma-

terial in the joint McGaw and Weckesser demonstrated the additional value of oxygen in the joint The original method of spreading the joint was a manual one and exposed the x-ray technician to unnecessary hazard Several new devices have been designed to accomplish this same result by mechanical means Such a device is shown in Figure 2, C and D The ankle and thigh are placed in bands, and the ankle is moved laterally, and then medially, about a block of wood placed along the lateral or medial margin of the knee joint (Fig 3) This widens the joint space on the opposite side of the block in turn for the separate exposures

In order to obtain a clear visualization of the menisci, it is important that the tibial plateau be perfectly perpendicular to the film In the average patient, this is

is supported perpendicular to the table top, anterior or posterior to the knee, as the case may be

A fluoroscopic spot-film technic has also been employed, and this method may be very satisfactory if an adequate film-target distance is employed. In the average case, however, this adjunct is unnecessary.

We feel that the routine examination should include both prone and supine studies and that other methods need be used only as accessories when the routine methods fail. The radiologist must treat each case as an individual problem, and check all films carefully until a diagnostic result is obtained, if the injection has been satisfactory. Occasionally every means at our disposal will be necessary. In the case of a poor injection, subcutaneous emphysema, or excessive fluid in the joint, which may interfere with visualization, one need not hesitate to repeat the entire procedure on another occasion.

THE NORMAL PNEUMOARTHROGRAM

The accompanying figures and diagrams (Fig 4, A, B, and C) show the structures of the knee as outlined on a normal pneumoarthrogram. The structures which can be clearly detected are the suprapatellar bursa, the infrapatellar fat pad, the medial meniscus (semilunar cartilage), the lateral meniscus, the popliteal bursa. Structures which can be delineated fairly well, but not sufficiently accurately for diagnosis, are the synovial reflection over the popliteus muscle, the crucial ligaments, the articular cartilage covering the femoral condyles, tibial condyles and the patella, the posterior septum.

A popliteal bursa (Baker's cyst) communicating with the posterior joint space is normally seen in about 13 per cent of cases, and apparently may or may not have pathological significance, depending upon whether or not it is subject to inflammation or obstruction at its neck. Inflating this bursa with oxygen is a definite aid in its surgical excision.

The Suprapatellar Bursa or Pouch. The suprapatellar bursa is best visualized on

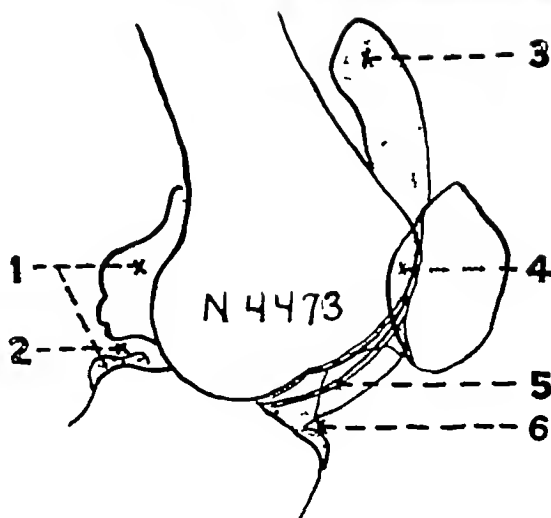


Fig 4 C. Direct lateral view and tracing of knee joint. 1 Posterior pouches 2 Posterior septum 3 Suprapatellar bursa 4 Cartilage of patella 5 Infrapatellar fat pad 6 Ligamentum mucosum

the lateral projection. However, when it contains a space-occupying lesion (not calcified) such as a synovioma, the latter may be seen quite distinctly on the postero-anterior projection as well (see p 689). In the lateral view, the suprapatellar bursa is seen as an ovoid structure above the patella, communicating with the rest of the joint. The bursa may have one or more thin folds passing through it (Fig 5, A), or it may be unilocular. The floor of the

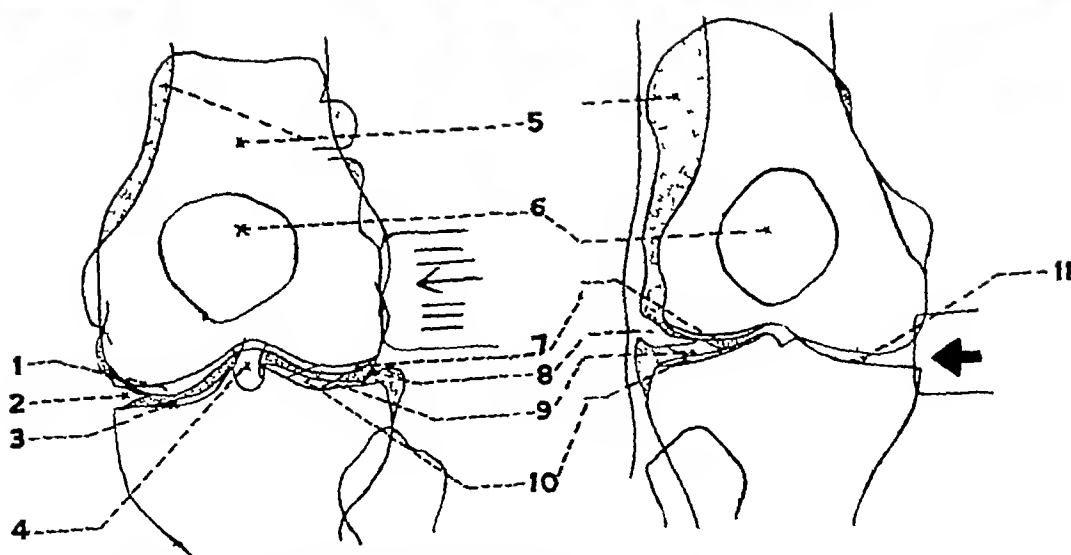
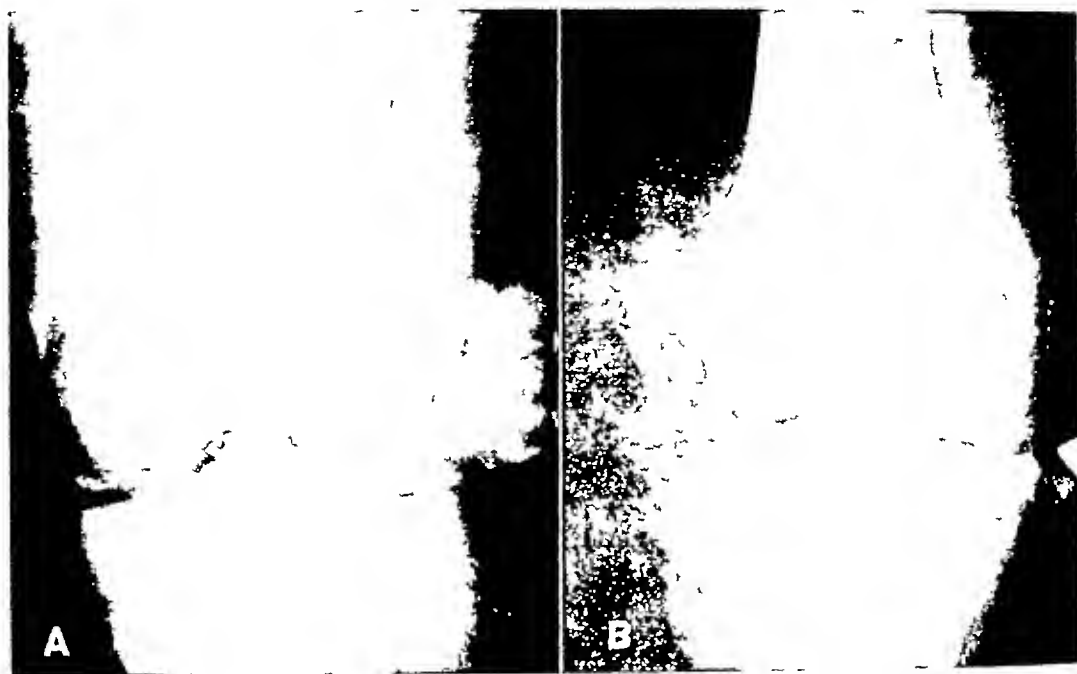


Fig 4, A and B Radiographic anatomy of the knee joint A View obtained by spreading the medial joint space. B View obtained by spreading the lateral joint space

The labeled drawings correspond with the roentgenograms above 1 Cartilage of medial femoral condyle 2 Medial meniscus 3 Cartilage of medial tibial condyle 4 Cruciate ligament 5 Suprapatellar bursa 6 Patella 7 Cartilage of lateral femoral condyle 8 Lateral meniscus 9 Popliteus muscle 10 Cartilage of lateral tibial condyle 11 Medial joint space

lateral view, 51 kv p, with other factors as above

When the usual supine and prone film studies fail to give a sufficiently accurate visualization of the menisci, excellent visualization can usually be obtained by

turning the knee on one side or the other, allowing the oxygen to rise to the top, spreading the knee in the usual fashion over a block which acts as a fulcrum, and directing the x-ray beam horizontally through the joint (Fig 3, E and F) The cassette

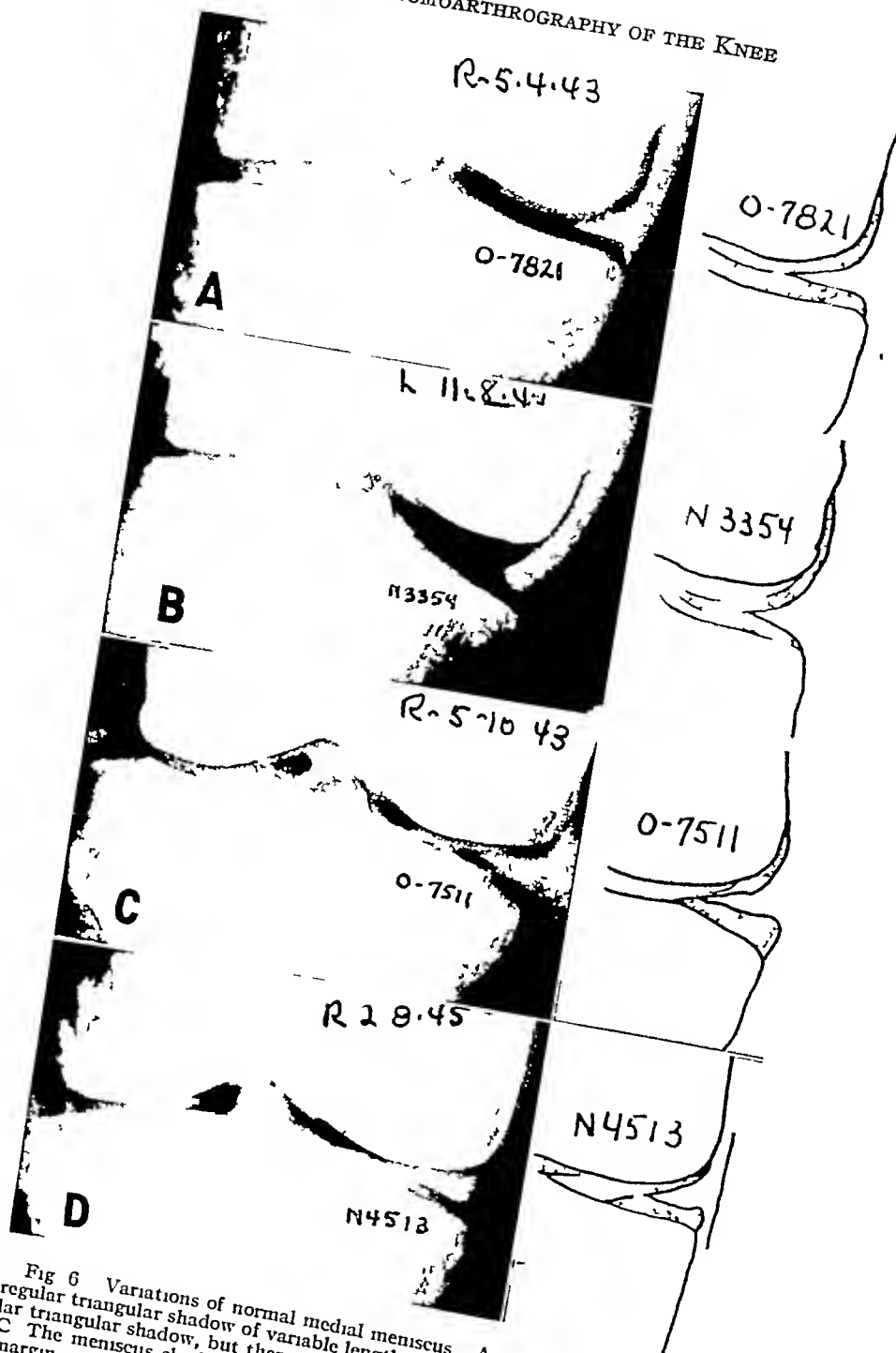


Fig 6 Variations of normal medial meniscus A The meniscus forms a regular triangular shadow of variable length B The meniscus forms a regular triangular shadow, but there is a laxity of the medial coronary ligament C The meniscus shadow has a somewhat undulating superior and inferior margin and is variable in length D The meniscus shadow has a small notch along the inferior margin of the base of the meniscus See also Fig 7

and the anterior articular surfaces of the condyles of the femur and the tibia Anteriorly, its shadow blends with that of the quadriceps tendon The portion which ex-

tends into the joint posteriorly (ligamentum mucosum) is pointed, but, as a rule, quite smooth The ligamentum mucosum is usually several millimeters superior and

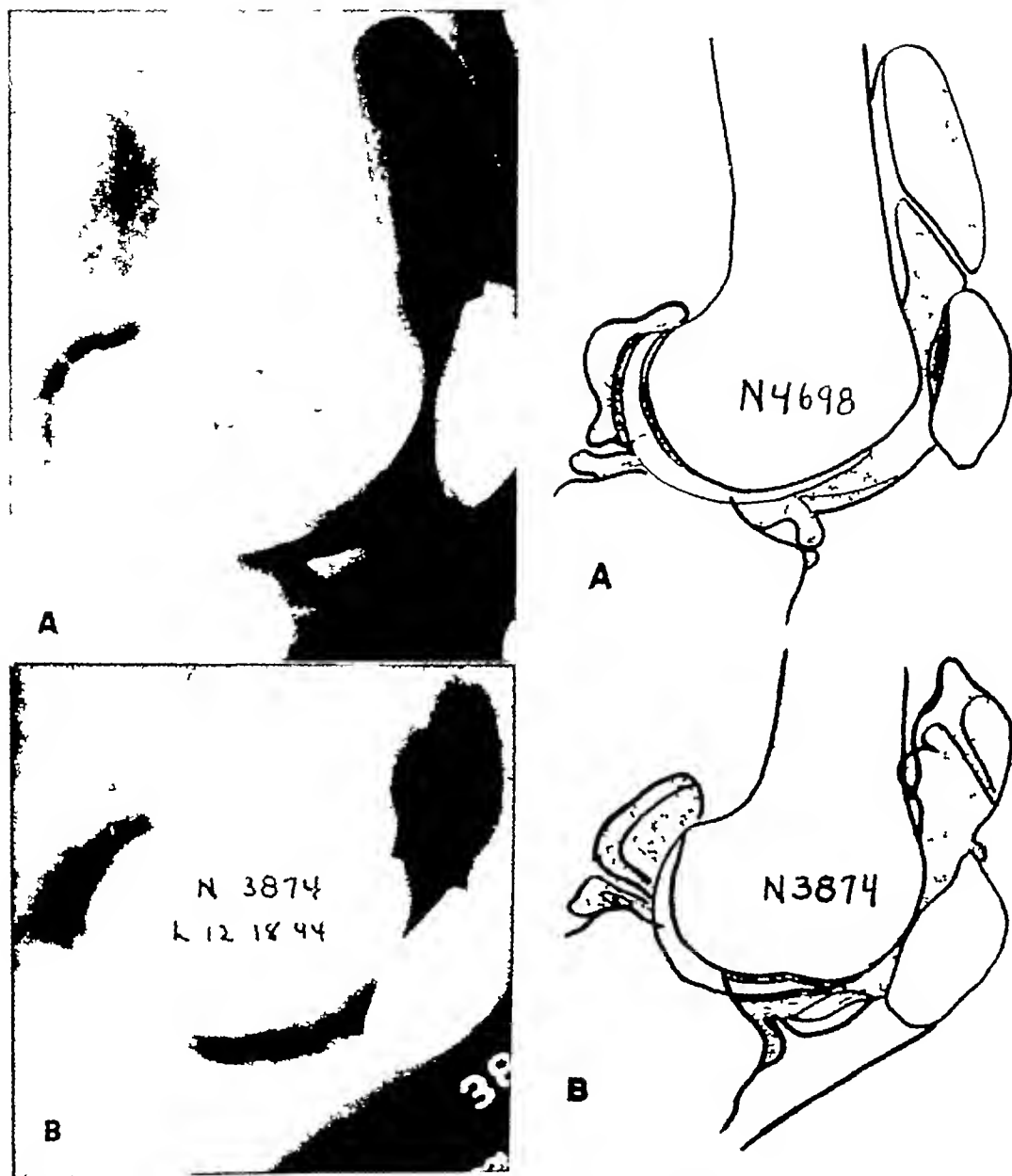


Fig 5 Variations of lateral view A Synovial fold frequently seen in suprapatellar bursa B Somewhat irregular but normal suprapatellar bursa

bursa may be straight or have a scalloped appearance due to loose areolar extra-synovial fat (Fig 5, B). It may vary in size considerably in the lateral projection, from 3.5 by 2.0 cm to 6.0 by 4.0 cm. In the postero-anterior (or anteroposterior) projection this structure when distended appears slightly wider than the distal end

of the shaft of the femur over which it is projected.

The Infrapatellar Fat Pad The infrapatellar fat pad is seen in the lateral view as a somewhat irregular triangular structure (Fig 4, C), which may have a double-contoured appearance, extending between the inferior articular margin of the patella

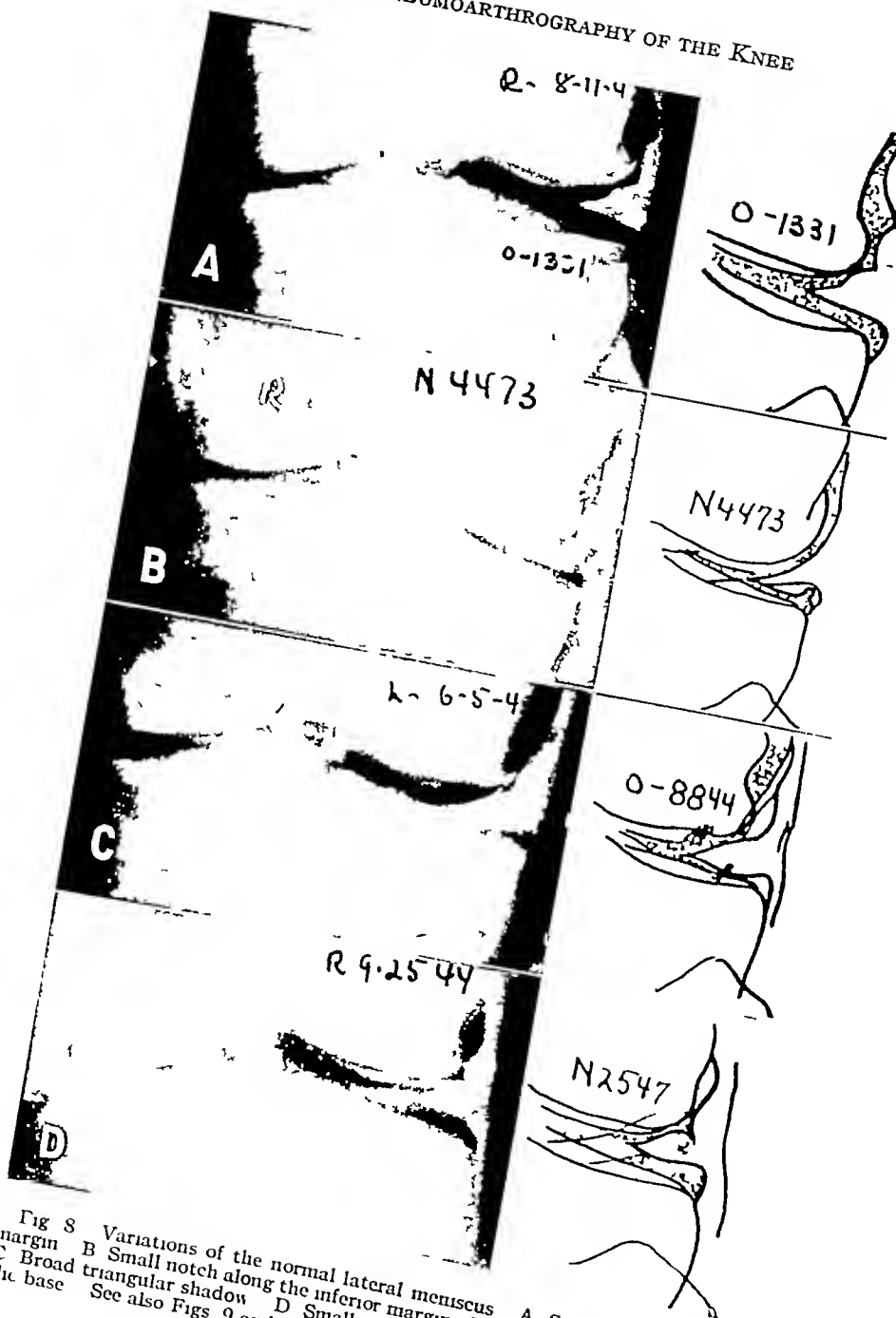


Fig 8 Variations of the normal lateral meniscus A Step like superior margin B Small notch along the inferior margin of the base of the meniscus C Broad triangular shadow D Small notch along the superior margin near the base See also Figs 9 and 10

fore attempting to determine the abnormal, even so, thus far, certain errors have been found to be inevitable These will be described in greater detail later

The Lateral Meniscus The lateral meniscus is seen to best advantage on those views where pressure is applied medially the lateral joint space is spread This

meniscus varies considerably in appearance Its attachment to the lateral coronary ligament is broader than that of the medial meniscus and, in contrast to the latter, there is usually an air shadow between the meniscus and the ligament, due to the fact that there is no capsular attachment where the synovia is reflected around

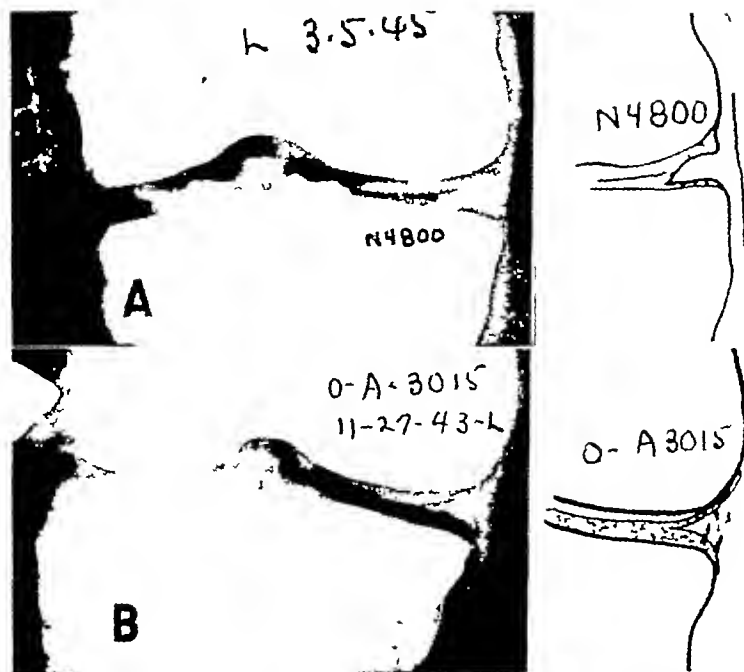


Fig 7 Further variations of normal medial meniscus A A small notch along the superior margin of the base of the meniscus B Extraneous air shadows overlying the shadow of the meniscus

posterior to the anterior margin of the tibial plateau. When viewed under a bright light, several rounded portions may be seen to be superimposed upon the posterior oblique margin of the pad. This appearance, when marked to the point of almost complete obliteration of the anterior joint air space, is indicative of hypertrophy, chronic inflammation, or interstitial hemorrhage (see p 689). The shadow of the pad is rather homogeneous, when occasionally it assumes a speckled appearance, inflammation is usually the cause. The pad measures, as a rule, about 2.0 by 3.5 cm in the lateral view.

The Medial Meniscus The medial meniscus is clearly demonstrated on all the views where the medial side of the joint is spread. Its posterior attachment in the vicinity of the posterior septum is demonstrable on the lateral view. Its normal appearance varies considerably, but within the confines of a fairly definite pattern. This structure as seen on the roentgenogram is a profile of its mid-portion. It is triangular (Fig 6), with its base firmly at-

tached to the medial collateral ligament of the knee joint. Its pointed apex (free margin) is projected in the joint space between the medial and femoral condyles. Its free surfaces are perfectly smooth. It measures 1.0 to 1.5 cm in length and 3.0 to 5.0 mm at its base. Its upper and lower surfaces are usually symmetrical and can be clearly demarcated from adjoining structures. Normally it has a definitely homogeneous density throughout.

The various limits of normal are difficult to describe and can be ascertained best by analyzing a large group of normal studies. This has been attempted in the accompanying illustrations (Figs 6 and 7). The medial coronary (collateral) ligament may be partially torn, and yet the meniscus may be entirely normal (Fig 6, B). The meniscus may vary in size and may have a somewhat undulating superior margin (Fig 6, C), it may be slightly notched at its base inferiorly (Fig 6, D), or superiorly (Fig 7, A). Extraneous air shadows may be projected over it (Fig 7, B). One must have a clear conception of the normal be-

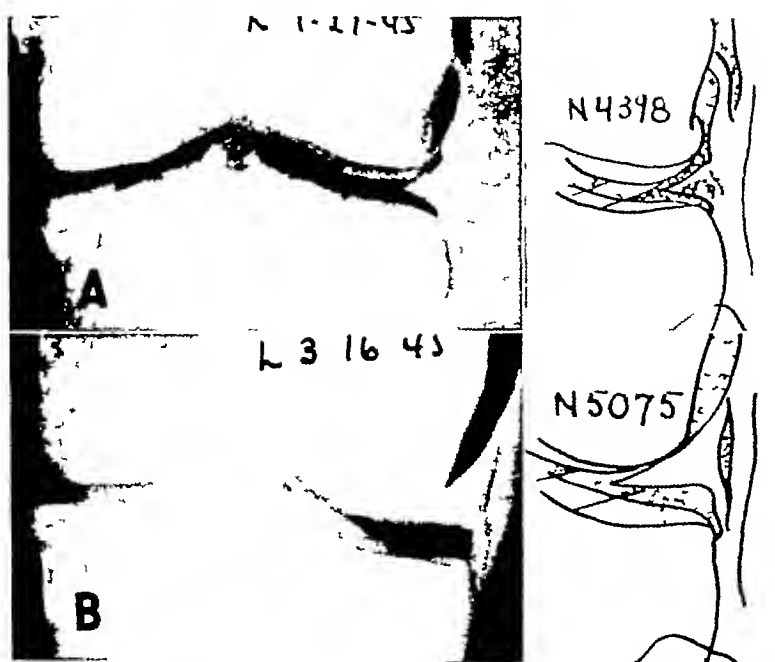


Fig 10 Further variations of the normal lateral meniscus A Irregular extraneous air shadows projected over the base of the meniscus shadow B Extra articular air shadow projected outside the base of the meniscus

oblique or transverse. Its superior margin may be step-like (Fig 8, A) instead of straight. There may be a small notch along the inferior margin near the base (Fig 8, B) or along the superior margin (Fig 8, D), or both inferiorly and superiorly near the base (Fig 9, A). A double-contoured appearance may result if more of the free edge is seen than in the usual transverse section. The meniscus may vary considerably as to size, but it is seldom very short normally (Fig 9, B).

There are also more confusing air shadows on the lateral side of the joint than are found medially (Fig 9, C and D, Fig 10, A and B). The popliteus muscle casts its shadow here and must be delineated. It not infrequently obscures the shadow of the free edge of the meniscus. The usual oblique shadow of the meniscus frequently overlaps the shadow of the lateral femoral condyle somewhat, but with good technic can be clearly shown. The shadow of the lateral meniscus is less apt to be as homogeneous as that of the medial meniscus.

Despite this great variety of normal appearances, our errors with regard to the lateral meniscus have been only slightly

more frequent than with regard to the medial. This is probably due to the fact that minimal changes in the appearance of the lateral meniscus are regarded as less significant than similar alterations in the appearance of the medial.

The Posterior Capsular Pouches The posterior capsular pouches are usually quite small with a linear septum extending obliquely through them. They are bilocular and projected directly between the posterior adjoining margins of the femoral and tibial condyles. The over-all measurements of the pouches are usually in the vicinity of 2.5 by 1.5 cm. We have never had occasion to diagnose abnormality of these structures *per se*.

A popliteal bursa or cyst (Fig 33), when present, usually communicates with the superior locule of the popliteal space by a narrow communication up to 1 cm in length. This structure may or may not contain fluid, and may be unilocular or multilocular. It varies considerably in size, anywhere from 1 cm to 5 or 6 cm in diameter. It may be ovoid, scalloped, or spherical in shape. It occurred in 13.5 per cent of all of our cases and is probably

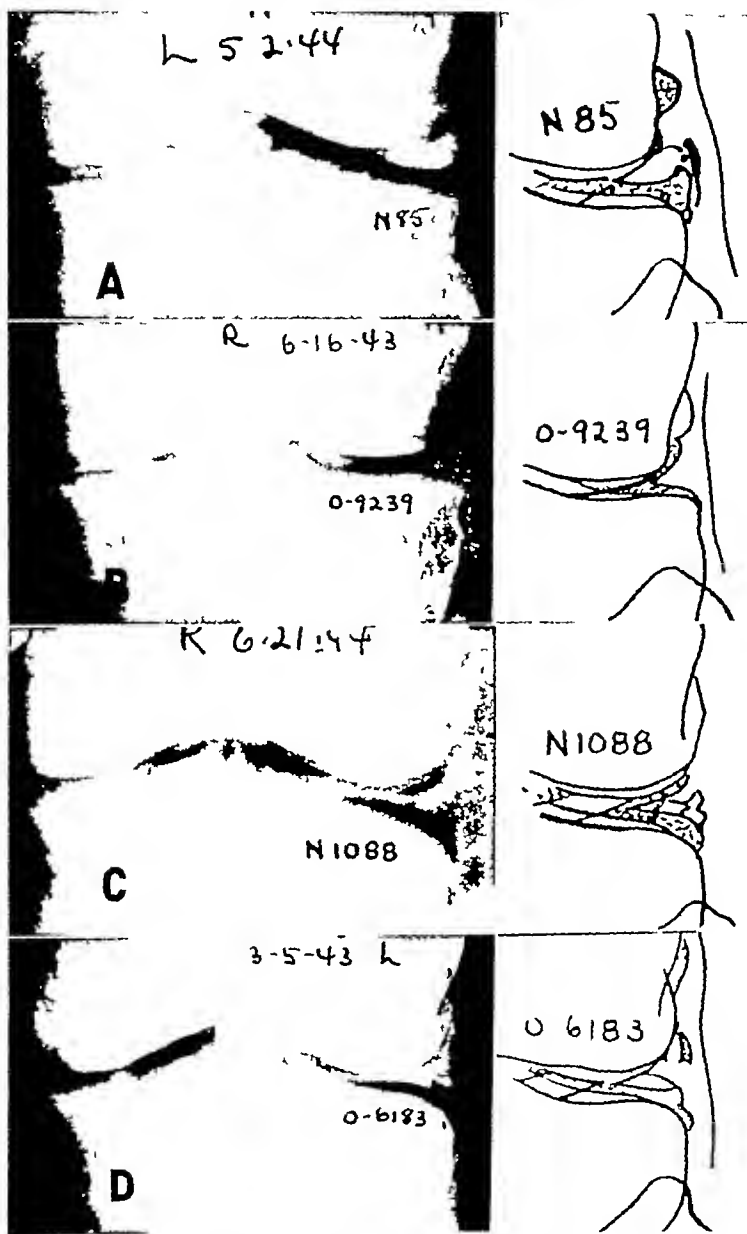


Fig 9 Further variations of the normal lateral meniscus A Small notch at both the superior and inferior margins of the base B Short, regular triangular shadow C Oblique extraneous air shadows projected over the meniscus shadow D Air shadow at the base of the meniscus

the popliteus muscle (Fig 9, D) This meniscus is usually more oblique in position, its base being superior to its free edge It is usually somewhat longer in profile view than the medial meniscus, and not quite so regular in contour (Figs 8 and 9)

The numerous variations of the normal

lateral meniscus are illustrated in Figures 8, 9, and 10 It will be noted that there may be a single or double air shadow at the base, or none at all Some of these air shadows are due to subcutaneous emphysema, while other shadows are more difficult to interpret The meniscus may be

inflammation or suppuration following an injury (Fig 31) and tumor (synovioma) (Fig 32)

Obliteration manifests itself as partial absence of the bursa or a speckled appearance. A certain amount of difficulty may be encountered in injection of the gas, and it is noted that the joint will take comparatively little oxygen, as little as 15 c.c. in one of our cases.

The synoviomias we have observed were visualized on both the postero-anterior and lateral projections as spherical structures about 1.5 cm. in diameter. These must be differentiated from those cases where the floor of the bursa appears slightly elevated or scalloped. In the latter instance, there is no abnormality detected in the postero-anterior projection, and this is used as the differentiating feature.

The Infrapatellar Fat Pad As the result of inflammation or fibrosis from one cause or another, there have been observed in the infrapatellar fat pad three general types of pathologic change which may be manifested on the films.

(1) The fat pad may appear larger than normal, as indicated by diminished oxygen in the infrapatellar region, due either to hypertrophy or fibrosis, chronic inflammation, hematoma, or contusion. In such instances, the appearance is that of an enlarged, scalloped structure with free fringes in the lateral view (Fig 29), and very little oxygen appears in the anterior joint space. It has been found that not all cases where the fat pad appears enlarged on the film prove to be abnormal at operation, *vice versa*, not all cases that are found to be abnormal at operation appear so on the film. It is hard to assay the accuracy of the radiographic diagnosis in these cases, since even at operation it is frequently difficult to determine whether or not the structure is abnormal. In any event, in the great majority of cases, abnormality of this fat pad is not in itself the major indication for arthrotony.

(2) The fat pad may be torn, with loose fringes lying free in the joint space (Fig 27).

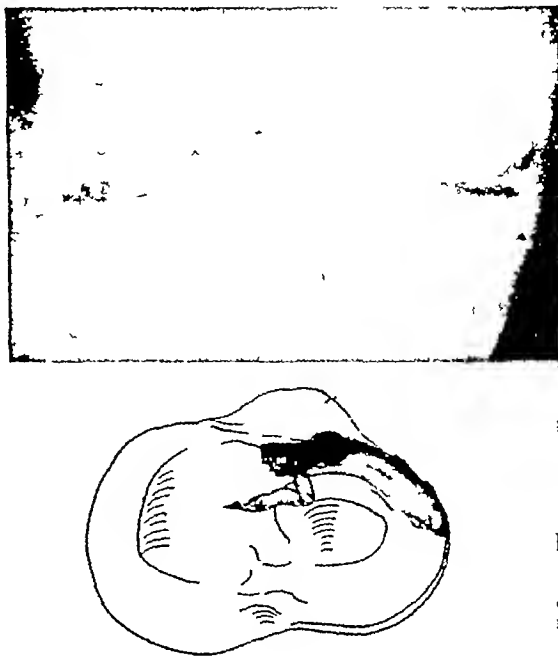


Fig 12 Dislocation-tear of meniscus. Actual specimen superimposed on a diagram of the tibial plateau and the corresponding roentgenogram. Only one-half of the meniscus was removed.

(3) A portion of the fat pad may be adherent to one of the cartilaginous structures in the knee joint as the end-result of inflammation (Fig 30). This diagnosis cannot be made with accuracy from film studies alone. If the ligamentum mucosum has a long fringe extending far into the anterior joint space, downward toward the tibia, this diagnosis is suggested.

Abnormalities of the fat pad are probably of symptomatic significance in many cases. In several instances in our series, these were the only findings at operation to explain the patients' complaints. These are usually cases with recurrent synovitis and no history of locking or clicking.

The Abnormal Medial Meniscus Fractures or tears can occur in any part of the medial meniscus, hence its abnormal appearance is extremely variable (Figs 12-15). In the great majority of cases, however, one has little difficulty in making the diagnosis, since the abnormal appearances fall into fairly definite patterns. Since the limits of normal are not so wide in the case of the medial meniscus as in the lateral, one can feel more secure in the diag-

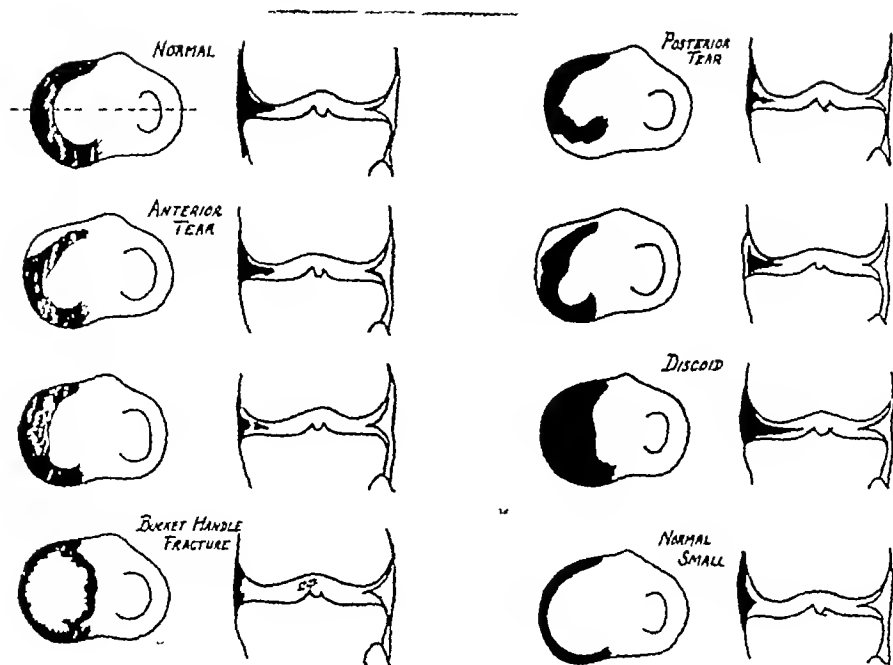


Fig 11 Comparison studies of menisci and appearance of pneumoarthrograms Top view of menisci and anteroposterior films

without pathological significance, unless it is subject to inflammation and its communication with the joint closes off intermittently. A popliteal cyst was removed in only 7 out of the 106 cases in which it was noted (6.6 per cent).

The Popliteus Muscle The popliteus muscle, covered by a synovial fold, may be seen on the postero-anterior and antero-posterior projections extending obliquely across the lateral joint space. Its usual measurements on these projections are 1.5 cm by 5.0 mm. Its shadow sometimes overlaps that of the free margin of the lateral meniscus, producing a confusing appearance if one is not aware of its presence. We have not detected any pathologic process in this structure.

The Crucial Ligaments The crucial ligaments are usually projected above the tibial spines in the anteroposterior and postero-anterior views. We have not been able to visualize these sufficiently distinctly to diagnose tears, although tears have been described by others. A chip fracture in the vicinity of the tibial spines has been found

to be associated with crucial tears on several occasions (see p. 697), but ordinary roentgenograms are better in this event than pneumoarthrograms.

Articular Cartilage Covering the Femoral, Tibial, and Patellar Condyles The cartilage overlying the femoral, tibial, and patellar condyles can be detected as a thin layer overlying the bony substance. In the case of the femoral and tibial condyles, this is usually 3 to 4 mm in width, varying roughly with age. The patellar cartilage, seen only on the lateral view, is thicker, the thickest portion being the mid-section, where it may measure as much as 8 mm.

We have one word of caution. Air shadows may actually interfere with accurate bony structure visualization. One should not use pneumoarthrograms as a substitute for plain roentgenograms of the knee.

THE ABNORMAL PNEUMOARTHROGRAM

The Suprapatellar Bursa Two types of abnormality have been observed in the suprapatellar bursa: obliteration, partial or almost complete, usually the result of

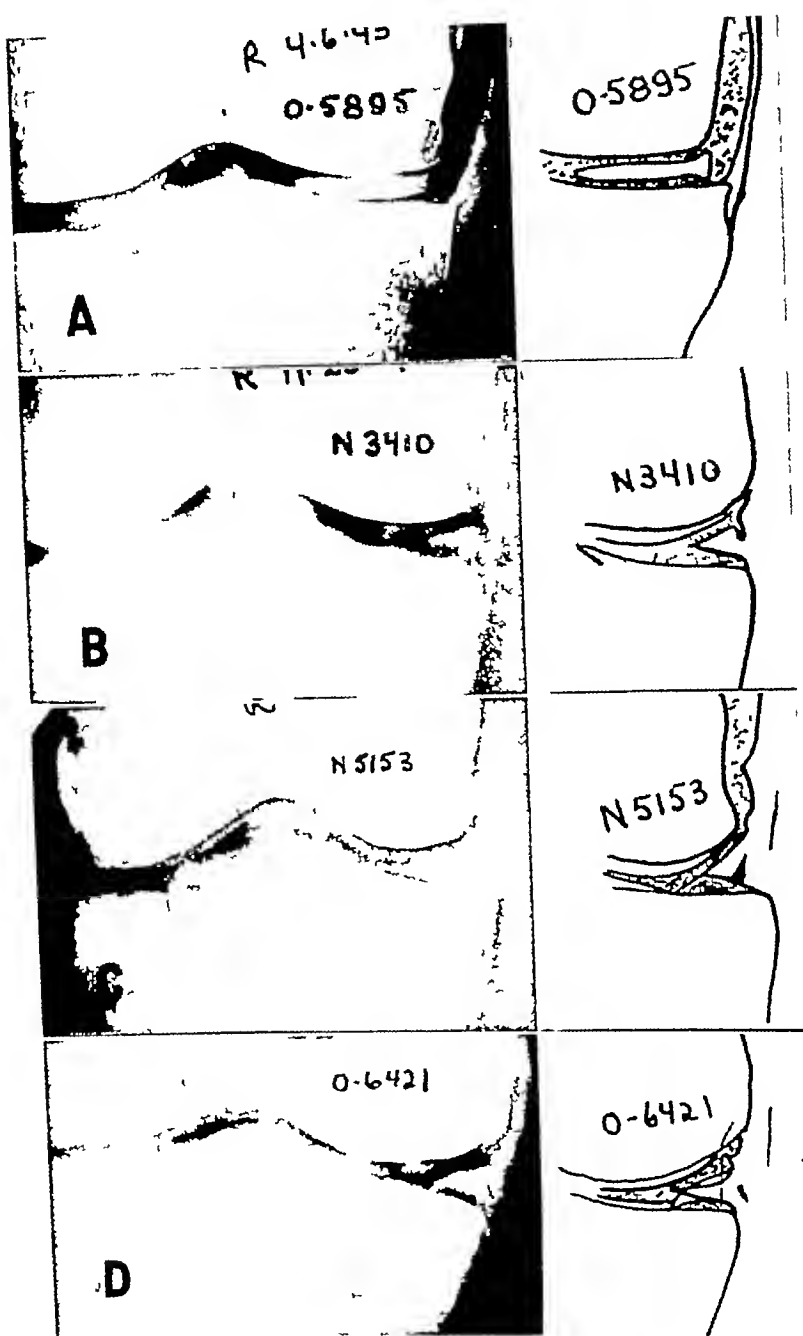


Fig 14 Further pathological variations in the medial meniscus A An obvious tear at the base of the meniscus shadow B A notching of the superior margin at the base of the meniscus due to an incomplete tear C Notching of the inferior margin of the base of the meniscus due to incomplete tear D The free margin of the meniscus shadow presents a crossed appearance

blunt (Fig 13, D) There may be a tear at the base of the meniscus (Fig 14, A) The meniscus may be partially torn along its superior attachment (Fig 14, B), or inferior attachment (Fig 14, C) The free

margin may show a crossing of fragments (Fig 14, D), or it may be rounded (Fig 15, A) There may be a fracture through the base of the meniscus shadow (Fig 15, B)

There are other appearances of the men-

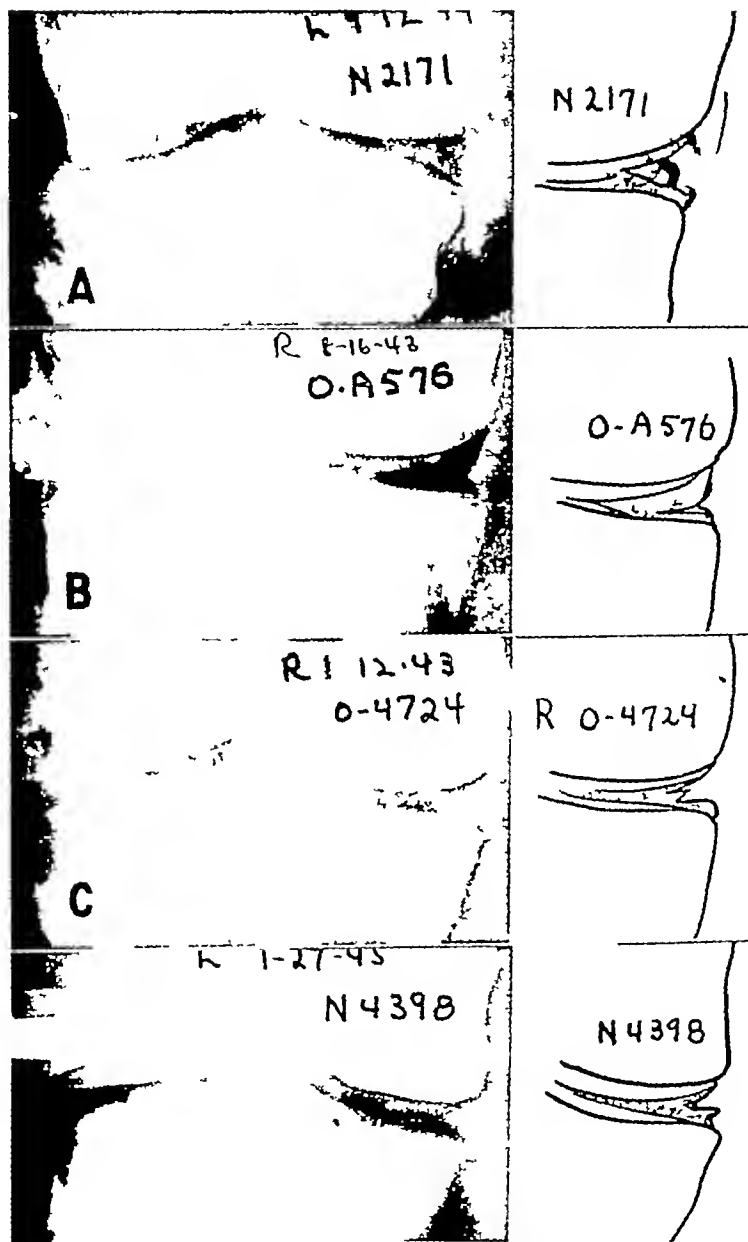


Fig 13 Pathological variations in the medial meniscus A The meniscus shadow is fragmented B The meniscus shadow is virtually absent indicating a fracture-dislocation of the bucket-handle type C The free edge of the meniscus is frayed and shortened D The meniscus shadow is short and blunt also indicating a bucket handle type of fracture See also Figs 14-16

nosis of medial meniscus abnormalities The accompanying comparison diagram (Fig 11) will prove helpful in visualizing the pathologic changes which are demonstrable roentgenographically

The meniscus shadow may appear frag-

mented as in Figure 13, A Its outline may be virtually absent due to fracture-dislocation of the meniscus, as in bucket-handle fractures (Fig 13, B) The free edge of the meniscus may appear frayed and shortened (Fig 13, C) or short and



Fig 16 Appearance of pneumoarthrogram after removal of the medial meniscus

anterior and anteroposterior projections (Figs 20 and 21), or the meniscus may appear normal on the one view and definitely abnormal on the other (Fig 20, A and B). Frequently, when a meniscus appears questionable the first time, a repeat examination at a later date will decide the issue quite definitely one way or another (Fig 22).

As previously indicated, our most frequent errors with regard to the medial meniscus pertain to fractures of the cornua, especially when this type of fracture is either anterior or posterior. Routine views which theoretically might show these fractures do so only if there is a secondary irregularity of the mid-section of the meniscus as well. Otherwise, the meniscus in these instances appears normal (Fig 34, A). Also, as previously indicated, the normal very short blunt meniscus simulates the appearance of the bucket-handle type of fracture (Fig 34, C). Fortunately, this type of anomaly is rare.

The Abnormal Lateral Meniscus As in the case of the medial meniscus, the abnormal lateral meniscus varies considerably in appearance. Due to the greater variation of the normal, however, and to interfering shadows, diagnosis of abnormality is more difficult.

The lateral meniscus may have irregular, serrated margins (Fig 17, A).

An air shadow at the base of the lateral meniscus is normal and, for this reason, some tears at the base of the meniscus will be missed. When this air shadow is ab-

normally wide, however, or incomplete, especially along the inferior margin of the base, it can be presumed to be abnormal, usually indicating a tear (Figs 17, B and 18, A).

As in the case of the medial meniscus, an absent or short blunt meniscus shadow is indicative of either dislocation-fracture (bucket-handle fracture) (Fig 17, C) or surgical excision (Fig 22, C and D), and the two conditions cannot be distinguished radiographically. The distinction is so readily made, however, by history and physical examination that it never presents much of a problem. Not all bucket-handle fractures have this appearance, they may assume other abnormal appearances, as described.

Fracture lines through any portion of the meniscus can also be detected. These may be vertical, horizontal, or oblique (Figs 17, D and 18, A).

The diagnosis of cyst of the lateral meniscus has been made on five occasions in our series (Figs 18, B and C). In one of these, the meniscus, in addition to being cystic, was also fractured (Fig 18, C). In these cases there is usually a palpable enlargement at the base of the meniscus laterally, and the radiographic diagnosis of the cyst is often corroborative, however, in one case, in an obese patient, the diagnosis was made radiographically and proved at operation, but could not be made by physical examination. The appearance is that of a broadening and bulging and generalized enlargement of the base of the meniscus.

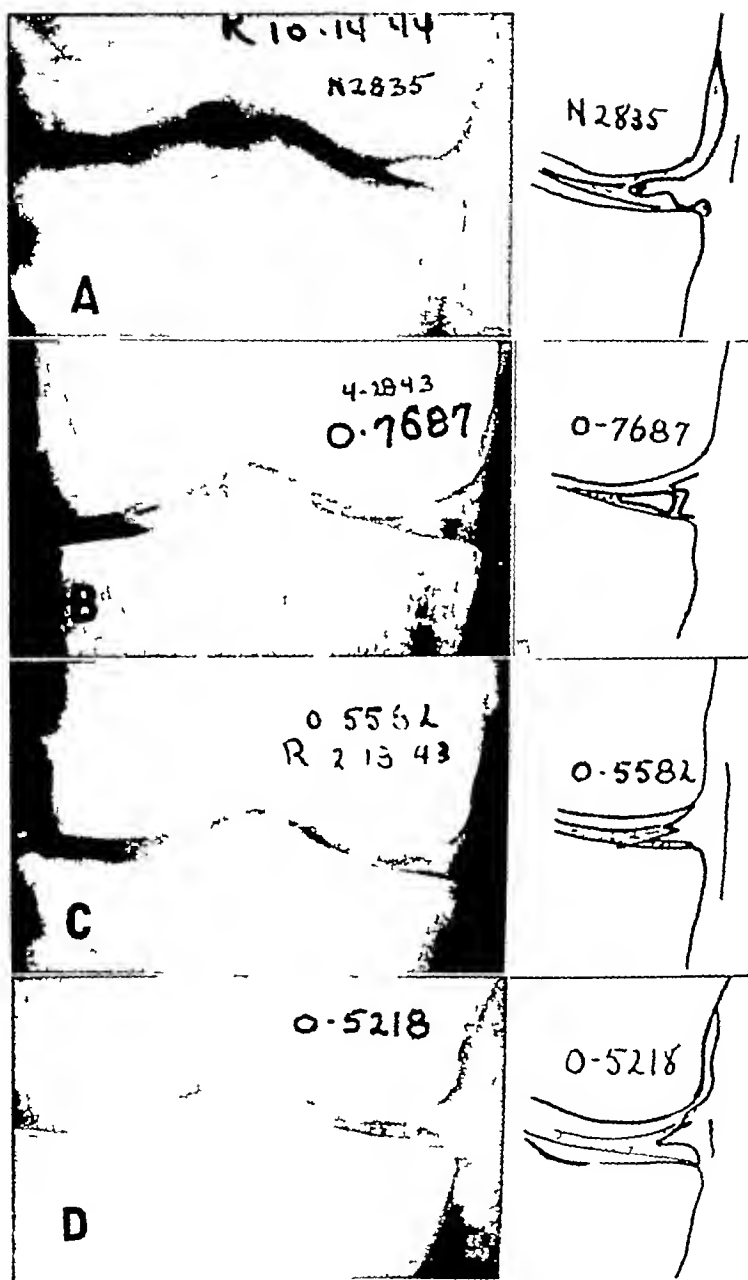


Fig 15 Further pathological variations in the medial meniscus. A Rounded appearance of the free margin of the meniscus indicating fraying. B Fracture through the base of the meniscus shadow. C The free margin of the meniscus presents a notched appearance. D The superior margin of the meniscus has a step like notched appearance with evidence of fracture.

iscus which indicate abnormality, but the exact pathology cannot always be predicted. The superior or inferior margin, or both, may appear irregular, jagged, and serrated (Fig 15, D). The apex of the

meniscus may have a serrated contour (Fig 15, C). The meniscus may also appear somewhat thinned-out and shortened.

Occasionally the type of abnormal appearance will be different on the postero-

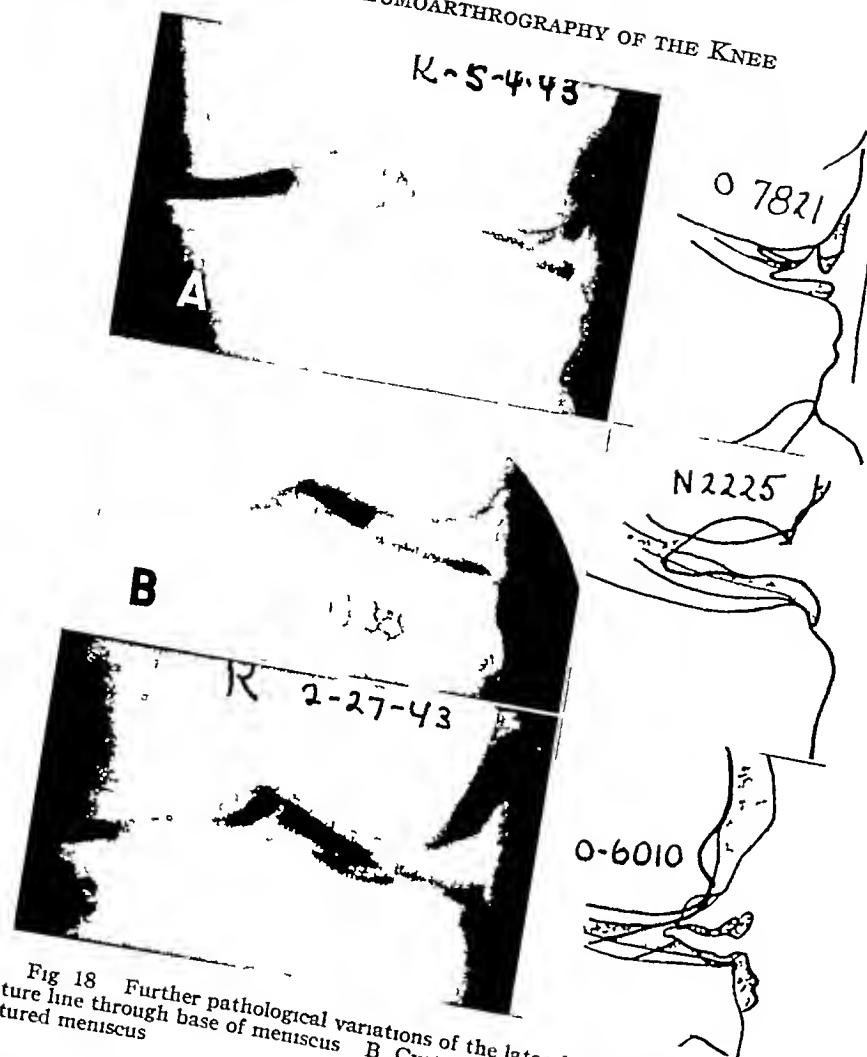


Fig 18 Further pathological variations of the lateral meniscus A Fracture line through base of meniscus B Cystic meniscus C Cystic and fractured meniscus

The lateral meniscus may appear different in anteroposterior and postero-anterior projections (Fig 21, C and D)

OSTEOCHONDritis DISSECANS AND CHONDROSIS

It is true that pneumoarthrograms rarely add to the diagnosis of osteochondritis dissecans (Figs 24 and 25) beyond what is already known from the plain films. The defect may, however, be accentuated by the air shadow and more readily detected. Also, the pneumoarthrogram shows the intrasynovial or extrasynovial position of the separated particles and their size.

Chondrosis of the patellar articular cartilage may be suggested in the roentgenogram by marked sclerosis and indentation

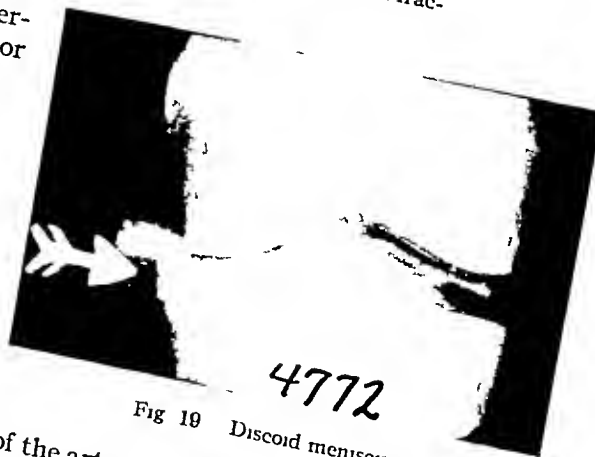


Fig 19 Discoid meniscus

of the articular margin and by thinning and irregularity of the cartilaginous shadow as seen on pneumoarthrograms. This diagnosis is not infrequently impossible to make under any condition.

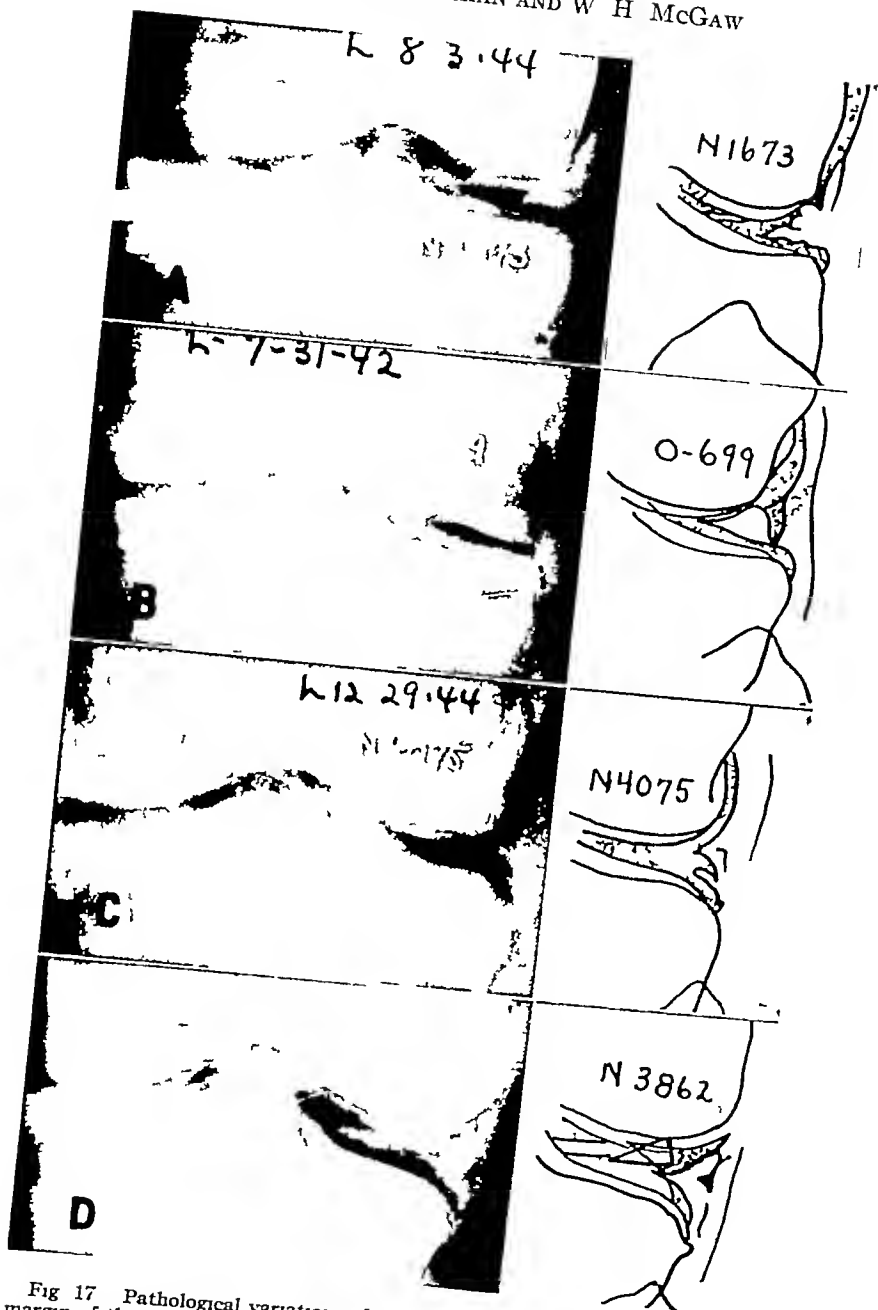


Fig 17 Pathological variations of the lateral meniscus A The superior margin of the shadow is irregular B Abnormally wide air shadow at base C The meniscus shadow is frayed and short—almost absent D Fracture lines traversing the shadow of the meniscus obliquely See also Figs 18 and 19

cus, and sometimes of other portions of the meniscus as well This finding is of surgical importance, since it indicates the extent of dissection necessary

A discoid meniscus appears elongated (Fig 19) Pathologically, these menisci are circular or plate-like (Fig 11) rather

than semilunar in shape, and therefore the transverse section seen on the radiograph extends about two-thirds or more across the tibial plateau on the side in question Ordinarily, the meniscus shadow occupies only about 50 per cent or less of the lateral or medial joint space

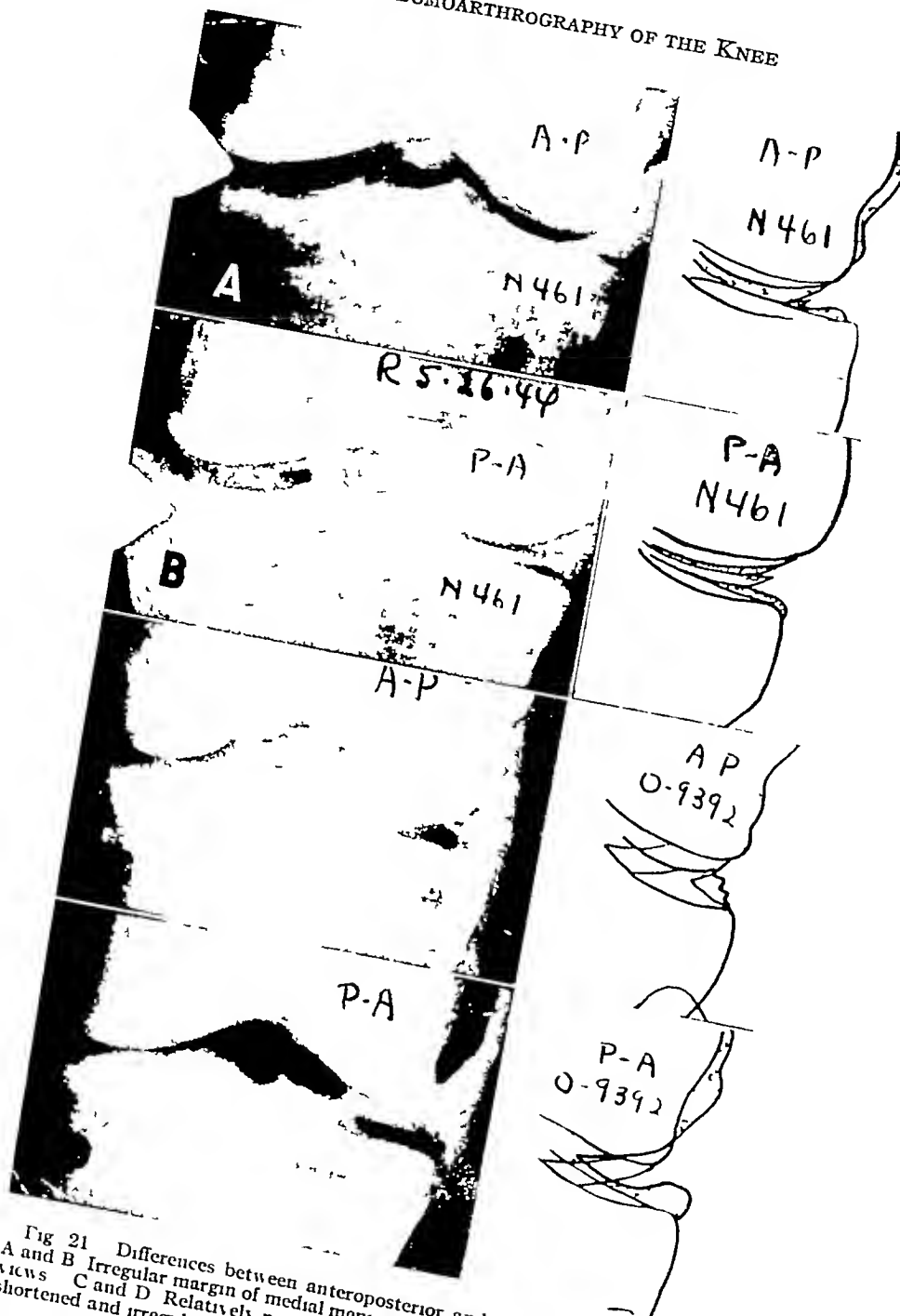


Fig 21 Differences between anteroposterior and postero-anterior views
A and B Irregular margin of medial meniscus appearing differently in the two
views C and D Relatively normal appearing lateral meniscus (D) seen as
shortened and irregular in anteroposterior view

ligaments have already been discussed. Apart from the appearance of chip fractures in the region of the tibial spines and an air bubble in the vicinity of the ligament, this diagnosis cannot be made radiographically with technic thus far described.

We have measured anterior and posterior displacement of the tibia with respect to the femur in the lateral knee films, but that is a subject quite apart from pneumoarthrography.

Crucial ligament tears occurred in 22

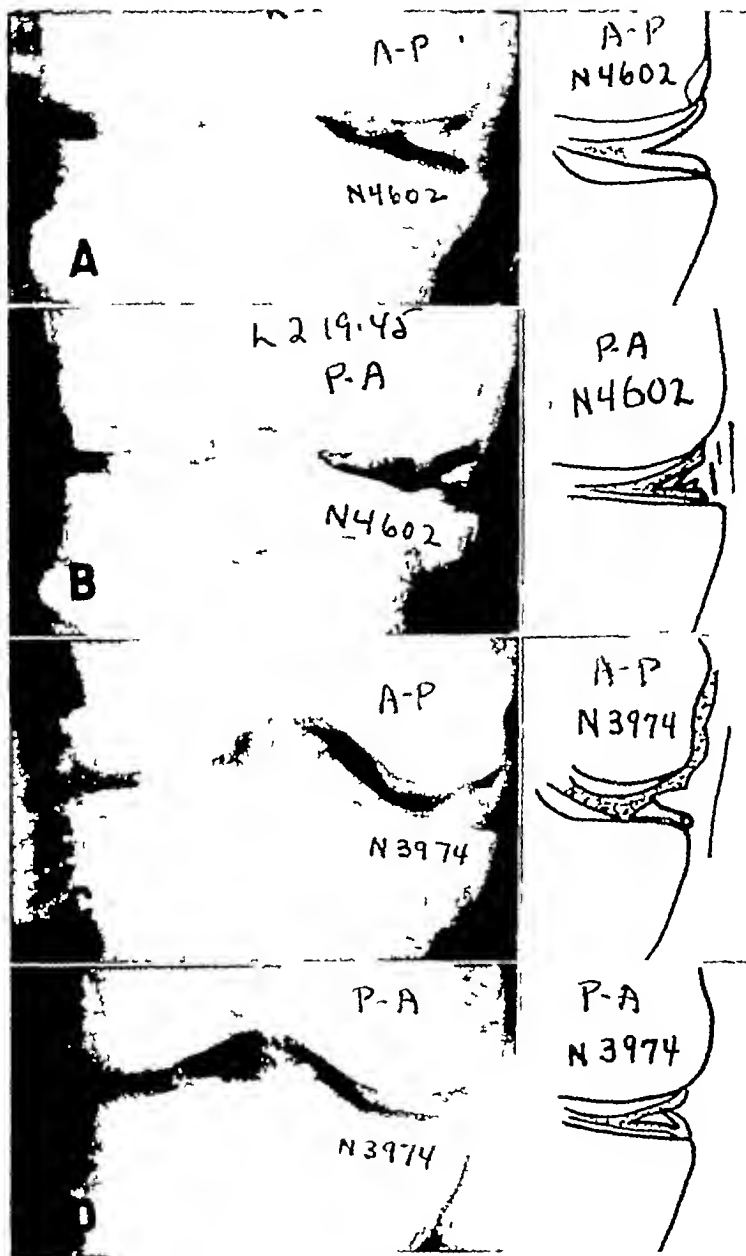


Fig 20 Differences between anteroposterior and postero-anterior views
 A Anteroposterior view showing normal appearing medial meniscus B
 Postero-anterior view showing irregular inferior margin C and D Antero
 posterior and postero anterior views showing difference in appearance of
 oblique fracture lines through body of medial meniscus

LIGAMENTOUS STRUCTURES

Relaxed medial and lateral coronary (collateral) ligaments can be readily demonstrated because of the spreading

technic (see abnormal medial spread in Fig 6, B) A fairly accurate basis for the diagnosis of relaxation of these ligaments can be achieved

The findings with regard to torn crucial

TABLE I GENERAL STATISTICS

	April 1942-44	April 1944-45	Total
Total pneumoarthrograms	528	254	782 (100 0%)
Operated pneumoarthrogram cases*	230	85	315 (40 3%)
Arthrotomies without previous pneumoarthrograms	34	6	40

*Forty arthrotomies were done without previous pneumoarthrograms for internal derangements, patellar fractures, and removal of foreign bodies

ization of the internal structures of the joint. We have found that compression bandages over the suprapatellar bursa are usually not necessary, but occasionally enhance the visualization of the menisci. It is best to wait, if possible, until all or most of the fluid is out of the joint before proceeding with the examination. The prone position in such cases usually yields better diagnostic results than the supine (Fig 23). The lateral position (tube horizontal) is also of value in such cases.

The hazy appearance in supine positions and the clear visualization in the prone furnish an excellent diagnostic criterion of fluid in the joint. In the prone position, the fluid flows into the suprapatellar bursa, leaving the joint space relatively clear.

STATISTICAL EVALUATION

General Statistics. The period of observation in the series here reported covers the three-year interval between April 1942 and April 1945, inclusive. The total number of pneumoarthrograms of the knee done in this period was 782 (Table I). In the first two-year period, 528 were done, and in the third year, 254. These two intervals are separated in order to determine more accurately the status of the pneumoarthrogram in its more recent stage of development. Only those operated cases have been studied in which pneumoarthrograms were made prior to operation. During the first two-year period, 230 arthrotomies were done on cases which had had pneumoarthrograms previously, and in the third-year period, 85, making a total of 315

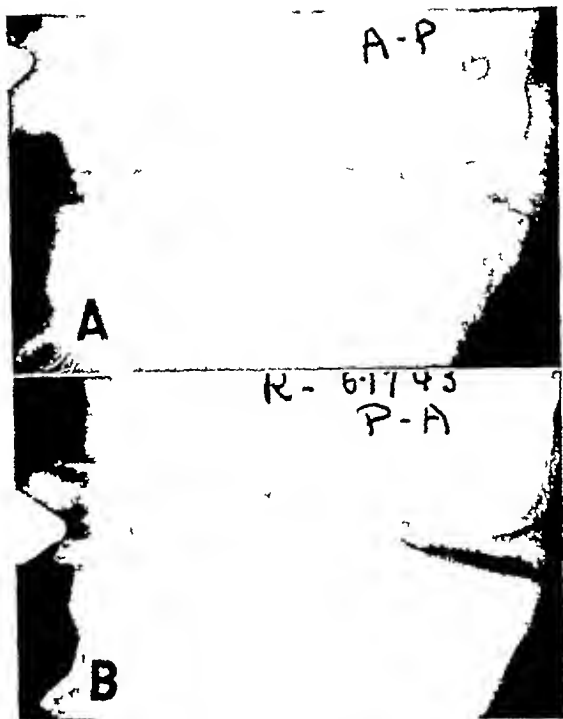


Fig 23 Appearance in hydrarthrosis. In the anteroposterior view (A) the structures appear blurred and indistinct. In the posteroanterior view (B), the fluid shifts to the suprapatellar bursa and the structures are much more distinct.

operated cases. Forty arthrotomies were done without previous pneumoarthrograms, a few for internal derangement, but the majority for patellar fractures and for the removal of loose bodies.

We have arbitrarily divided the surgical findings at arthrotomy into two types: (a) a major type, where the designated finding was the most significant or sole finding at operation; (b) a minor type, where the described findings were of lesser importance and in every case occurred with some other finding classified under the major type. Arthrotomies were done because either the clinical or radiographic findings suggested a good prognosis.

In certain cases there were two findings which were considered of major significance. Thus, in 10 cases two abnormal menisci were found either in the same or different knees (Table II). In 4 additional cases other miscellaneous findings made two major diagnoses necessary in each instance. This is very important surgi-

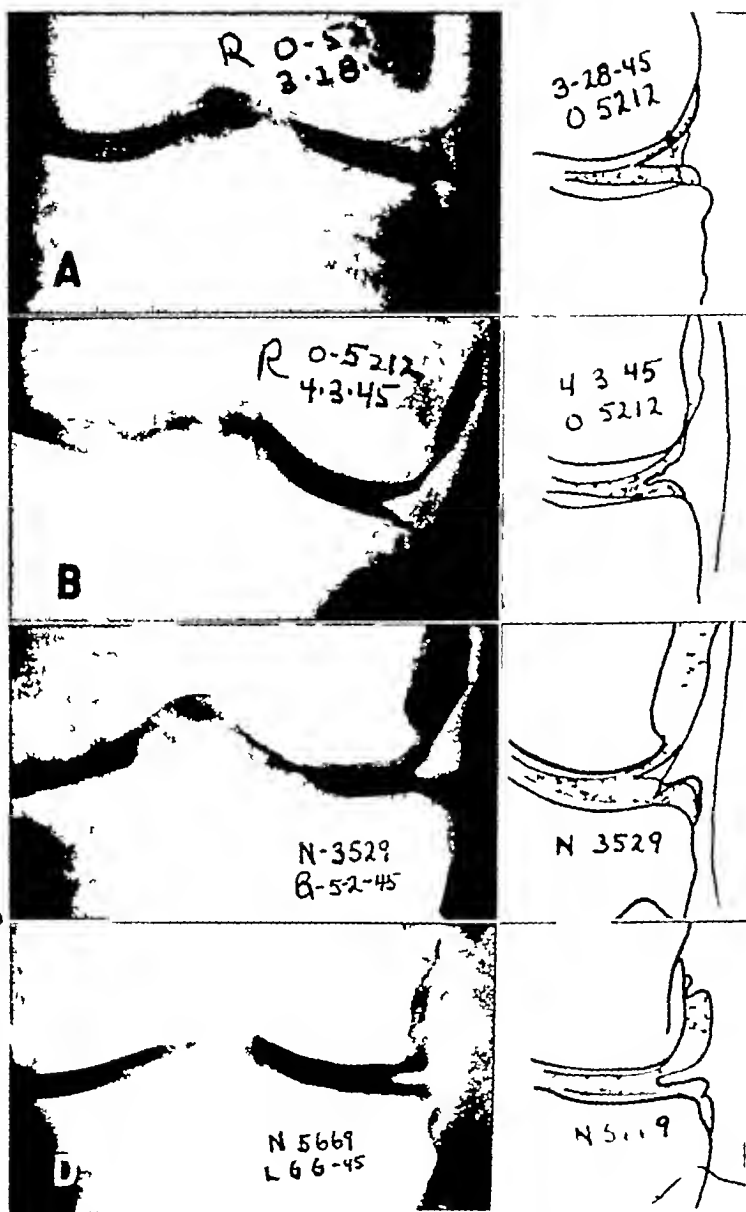


Fig 22 Changes in appearance of medial meniscus shadow with the passage of time A Superimposed air shadow—not definitely abnormal B Irregular, frayed meniscus shadow at a later date. C and D Appearance after the removal of lateral menisci, simulating fracture-dislocation of the bucket handle type

cases, or 6.9 per cent of the 315 patients operated upon in our series, usually in combination with meniscal fractures, since this abnormality by itself was not considered adequate indication for arthrotomy in an overseas Army hospital. It occurred alone, with no other demonstrable abnormality, in only 4 cases, or 1.3 per cent

FLUID IN THE JOINT SPACE

In the presence of a hydroarthrosis, as much fluid as possible should be removed from the knee joint prior to oxygen insufflation. At best, however, a small amount of fluid retention is inevitable, and this may interfere with the accurate visual-

TABLE III TOTAL INCIDENCE OF LESIONS IN OPERATED CASES WITH PNEUMOARTHROGRAMS (APRIL 1942-APRIL 1945)

	Major Findings	Lesser Findings	Total	% of 524	% of 315
Abnormal medial meniscus	155	0	155	29 8	49 2
Abnormal lateral meniscus	63	0	63	12 0	20 0
Abnormal fat pad	32	65	97	18 5	30 8
Popliteal cyst	7	41	48	9 1	15 2
Loose bodies without osteochondritis or chondrosis	7	1	8	1 5	2 5
Osteochondritis dissecans and chondrosis	39	41	80	15 2	25 4
Medial femoral condyle	(15)	(21)	(36)		
Lateral femoral condyle	(4)	(6)	(10)		
Patella	(20)	(14)	(34)		
Generalized	(2)	(7)	(9)		
With loose bodies	(19)	(3)	(22)		
Arthritis	11	29	40	7 6	12 7
Crucial ligament tears	4	18	22	4 2	7 0
Miscellaneous	11	0	11	2 1	3 5
Synovioma	(1)				
Obliterated bursa	(1)				
Normals	(8)				
Questionable findings	(1)				
Total	329	195	524	100 0	
No cases involved	315	158	315		

TABLE IV ACCURACY OF PNEUMOARTHROGRAMS IN RELATION TO MAJOR SURGICAL FINDINGS

Classification	April 1942-44			April 1944-45			Total		
	No Cases	No Major Findings	Per cent	No Cases	No Major Findings	Per cent	No Cases	No Major Findings	Per cent
A Diagnosis definitely suggested	127	134	55 3	66	67	77 0	193	201	61 1
B Diagnosis partially correct	22	23	9 5	3	4	4 6	25	27	8 2
TOTAL A + B	149	157	64 8	69	71	81 6	218	228	69 3
C Unsatisfactory examinations	33	35	14 5	2	2	2 3	35	37	11 2
D Mistaken diagnoses	48	50	20 7	14*	14*	16 1	62	64	19 4
TOTAL C + D	81	85	35 2	16	16	18 4	97	101	30 6
General Totals (A + B + C + D)	230	242	100 0	85	87	100 0	315	329	99 9

* Lesion diagnosed on wrong side in two cases making really two more errors than indicated for this period

per cent) and these would also fall into this latter category

Single miscellaneous findings included a synovioma, an obliterated suprapatellar bursa, and one case in which a questionable finding of an abnormally loose medial meniscus was noted

It is interesting to note the following total incidence of lesions in the knee (without regard to whether they were considered major or lesser findings) abnormal fat pad, 30 8 per cent, loose bodies without osteochondritis, 2 5 per cent (considered major in all but one case), osteochondritis or chondrosis, 25 4 per cent, arthritis, 12 7

per cent, crucial ligament tears, 7 0 per cent, popliteal cysts, 15 2 per cent, as previously indicated. More than one pathologic significant change was thus found in 158 of the 315 cases, or approximately one-half (Table III)

General Accuracy of the Pneumoarthrograms in Relation to the Diagnosis of the Major Surgical Finding (Table IV) We have considered the first two-year interval as separate from the third year in order to gain some idea of the improvement achieved as the result of experience in interpretation and improvements in technic. The pneumoarthrograms have been divided



Fig 24 Appearance in osteochondritis dissecans Oxygen enters the defect in the medial femoral condyle and produces intensification of the defect. The medial meniscus is also pathological

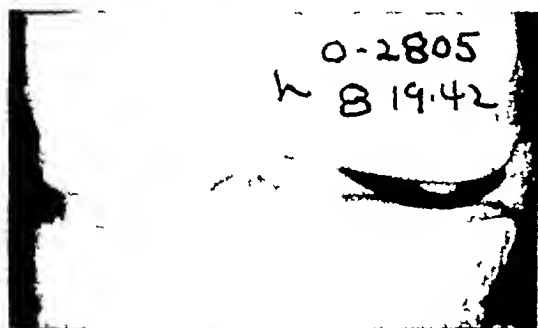


Fig 25 Osteochondritis dissecans Slight intensification of the defect in the medial femoral condyle by the oxygen The medial meniscus in this case is normal

cally and shows the great value of pneumoarthrograms at times, since it is impossible clinically to diagnose a bilateral meniscus tear in the same knee. The procedure also aids materially in preventing the missing of multiple pathologic findings.

In cases of osteochondritis dissecans where a fractured meniscus was also found, the fracture was listed as the major diagnosis unless the osteochondritis was very severe, because, by and large, the pneumoarthrogram is not necessary for a diagnosis of the latter disease.

Thus, in the total 315 cases, because of the duplication of diagnoses in 14, the total number of major pathologic diagnoses was 329: 242 during the first two-year interval and 87 in the third year (Table II).

Incidence of Lesions in Operated Cases with Pneumoarthrograms An abnormal meniscus was found in 218 cases, 69.2 per cent of the total number of major diagnoses made (Table III). Abnormal medial menisci numbered 155, whereas the lateral

numbered 63, a ratio of approximately 5 to 2, or 47.1 per cent as against 19.1 per cent.

Chondrosis of the patella and osteochondritis dissecans were considered major diagnoses in 39 cases, or 11.9 per cent. Loose bodies occurred in 19 of these. The medial femoral condyle was involved in 15, the lateral in 4, and there was a chondrosis of the patella in 20. The high incidence of patellar chondrosis is significant.

Seven popliteal cysts were operated upon, accounting for only 2.1 per cent of the major diagnoses, despite the relatively high incidence of popliteal bursae in general.

TABLE II CASE DISTRIBUTION OF PATHOLOGIC DIAGNOSES

	April 1942-44	April 1944-45	Total
Total major pathologic diagnoses	242	87	329
Total cases	230	85	315
Cases with more than one major finding	12	2	14
With abnormal menisci	9	1	10
With 2 miscellaneous abnormalities	3	1	4

Loose bodies without demonstrable osteochondritis or chondrosis were considered major findings in 2.1 per cent of the cases.

Arthritis (without other derangement) was the major finding in 3.3 per cent of the series. Crucial ligament tears were the only finding in 1.2 per cent, and an abnormal fat pad in 9.7 per cent. Cases in these three categories were usually treated surgically, with a preoperative diagnosis of some other type of internal derangement. Eight normal knees were operated on (2.4

TABLE III TOTAL INCIDENCE OF LESIONS IN OPERATED CASES WITH PNEUMOARTHROGRAMS
(APRIL 1942-APRIL 1945)

	Major Findings	Lesser Findings	Total	% of 524	% of 315
Abnormal medial meniscus	155	0	155	29.8	49.2
Abnormal lateral meniscus	63	0	63	12.0	20.0
Abnormal fat pad	32	65	97	18.5	30.8
Popliteal cyst	7	41	48	9.1	15.2
Loose bodies without osteochondritis or chondrosis	7	1	8	1.5	2.5
Osteochondritis dissecans and chondrosis	39	41	80	15.2	25.4
Medial femoral condyle	(15)	(21)	(36)		
Lateral femoral condyle	(4)	(6)	(10)		
Patella	(20)	(14)	(34)		
Generalized	(2)	(7)	(9)		
With loose bodies	(19)	(3)	(22)		
Arthritis	11	29	40	7.6	12.7
Crucial ligament tears	4	18	22	4.2	7.0
Miscellaneous	11	0	11	2.1	3.5
Synovium	(1)				
Obliterated bursa	(1)				
Normals	(8)				
Questionable findings	(1)				
Total	329	195	524	100.0	
No cases involved	315	158	315		

TABLE IV ACCURACY OF PNEUMOARTHROGRAMS IN RELATION TO MAJOR SURGICAL FINDINGS

Classification	April 1942-44			April 1944-45			Total		
	No Cases	No Major Findings	Per cent	No Cases	No Major Findings	Per cent	No Cases	No Major Findings	Per cent
A Diagnosis definitely suggested	127	134	55.3	66	67	77.0	193	201	61.1
B Diagnosis partially correct	22	23	9.5	3	4	4.6	25	27	8.2
TOTAL A + B	149	157	64.8	69	71	81.6	218	228	69.3
C Unsatisfactory examinations	33	35	14.5	2	2	2.3	35	37	11.2
D Mistaken diagnoses	48	50	20.7	14*	14*	16.1	62	64	19.4
TOTAL C + D	81	85	35.2	16	16	18.4	97	101	30.6
General Totals (A + B + C + D)	230	242	100.0	85	87	100.0	315	329	99.9

* Lesion diagnosed on wrong side in two cases making really two more errors than indicated for this period

per cent) and these would also fall into this latter category

Single miscellaneous findings included a synovium, an obliterated suprapatellar bursa, and one case in which a questionable finding of an abnormally loose medial meniscus was noted

It is interesting to note the following total incidence of lesions in the knee (without regard to whether they were considered major or lesser findings) abnormal fat pad, 30.8 per cent, loose bodies without osteochondritis, 2.5 per cent (considered major in all but one case), osteochondritis or chondrosis, 25.4 per cent, arthritis, 12.7

per cent, crucial ligament tears, 7.0 per cent, popliteal cysts, 15.2 per cent, as previously indicated. More than one pathologic significant change was thus found in 158 of the 315 cases, or approximately one-half (Table III)

General Accuracy of the Pneumoarthrograms in Relation to the Diagnosis of the Major Surgical Finding (Table IV) We have considered the first two-year interval as separate from the third year in order to gain some idea of the improvement achieved as the result of experience in interpretation and improvements in technique. The pneumoarthrograms have been divided

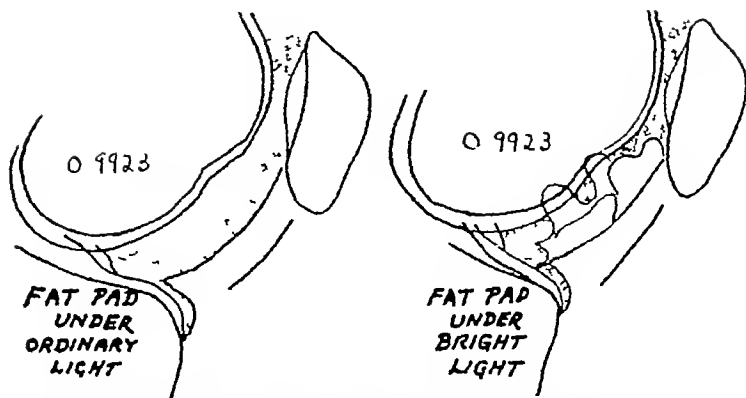


Fig 26 Pathological infrapatellar fat pads The lateral film must frequently be viewed under a bright light to reveal the lesion

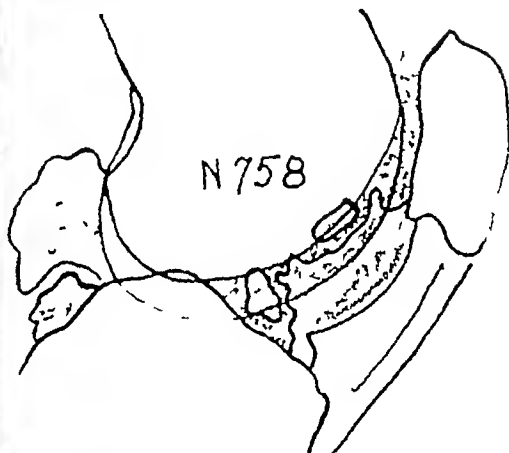


Fig 27 Infrapatellar fat pad frayed with loose fragments

into four groups. In Group A the correct diagnosis was definitely suggested, in Group B the diagnosis was partially correct, in Group C examination was unsatisfactory due to faulty technique either surgical or radiographic, in Group D an erroneous or misleading diagnosis was made. The classification is slightly different from that of McGaw and Weckesser in that any case in which the correct diagnosis was suggested was included in Group A, whether or not the statement was made in a positive manner, and any error, of commission or omission, was put in Group D.

In the first two-year interval, Group A comprised 55.3 per cent of the total, Group B, 9.5 per cent, Group C, 14.5 per cent, and

Group D, 20.7 per cent. In the third year, Group A increased to 77 per cent, Group B diminished to 4.6 per cent, there was a marked diminution in Group C to 2.3 per cent, and Group D was reduced to 16.1 per cent. The reason for the marked diminution in Group C was not only an improvement in radiographic and surgical technique, but also a repetition of the entire examination when necessary, until a satisfactory result was obtained. Usually a second examination was sufficient if the first failed. In one or two cases a third examination was required. Technical improvements accounted to a great extent for the diminution in Groups B and C, many of these being transferred to Group A.

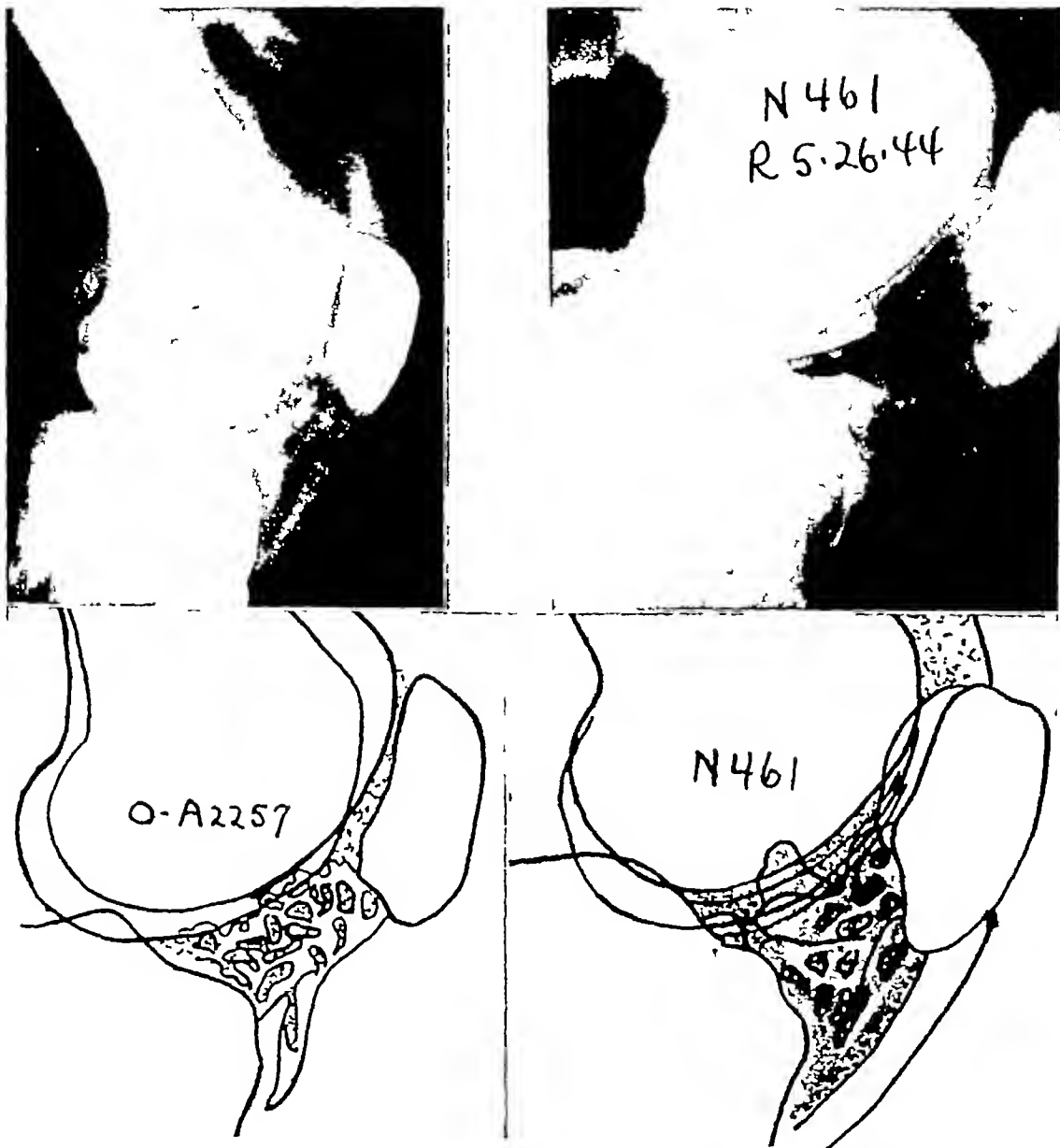


Fig 28 Hypertrophied fat pads with numerous synovial tags

The number of definitely misleading or erroneous diagnoses actually diminished relatively slightly. It will be noted from the analysis of errors below that these mistaken diagnoses fall to a great extent into a few groups, in which we have not as yet completely overcome the difficulties in arriving at an accurate diagnosis.

It is to be noted that in the third year the procedure was 81.6 per cent accurate. The over-all accuracy for the three-year

period is not nearly so good. Group A, 61.1 per cent, Group B, 8.2 per cent, Group C, 11.2 per cent, Group D, 19.4 per cent.

Relative Accuracy of Clinical Examination Without Reference to Radiographic Studies (Table V). For analyzing the accuracy of the clinical diagnoses, the cases are divided into five groups. In Group A the findings were typical of internal derangement injury with swelling,

TABLE V ACCURACY OF CLINICAL EXAMINATION ALONE IN RELATION TO MAJOR SURGICAL FINDINGS

Classification	April 1942-44			April 1944-45			Total		
	No Cases	No Major Findings	Per Cent	No Cases	No Major Findings	Per Cent	No Cases	No Major Findings	Per Cent
A Diagnosis definitely suggested	106	111	45.9	44	46	52.9	150	157	47.7
B Diagnosis partially suggested	56	59	24.4	19	19	21.8	75	78	23.7
TOTAL A + B	162	170	70.3	63	65	74.7	225	235	71.4
C Diagnosis not evident	13	16	6.6	3	3	3.4	16	19	5.8
D Definitely misleading	34	35	14.5	12	12	13.8	46	47	14.3
TOTAL C + D	47	51	21.1	15	15	17.2	62	66	20.1
E Data Poor	21	21	8.6	7	7	8.0	28	28	8.5
GENERAL TOTALS (A + B + C + D + E)	230	242	100.0	85	87	99.9	315	329	100.0

TABLE VI ACCURACY OF COMBINED DATA (CLINICAL AND PNEUMOARTHROGRAPHIC)

Classification	April 1942-44			April 1944-45			Total		
	No Cases	No Major Findings	Per Cent	No Cases	No Major Findings	Per Cent	No Cases	No Major Findings	Per Cent
1 Diagnosis suggested by both	95	101	41.7	53	55	63.2	148	156	47.4
2 Both misleading or poor	14	15	6.2	6	6	6.9	20	21	6.4
3 Pneumoarthrograms accurate, clinical studies not	35	37	15.3	9	9	10.3	44	46	14.0
4 Clinical studies accurate pneumoarthrograms not	65	68	28.1	10	10	11.5	75	78	23.7
5 Pneumoarthrograms accurate, clinical data inadequate	19	19	7.8	7	7	8.0	26	26	7.9
TOTAL COMBINED DATA ACCURATE	214	225	92.9	79	81	93.0	293	306	93.0
6 Pneumoarthrograms misleading, clinical data inadequate	2	2	0.8	0	0	0.0	2	2	0.6
TOTAL	230	242	99.9	85	87	99.9	315	329	100.0

pain, localized tenderness over the joint, locking, catching or clicking of the joint, with much disability. In Group B the findings were fairly suggestive of internal derangement; there was no history of locking, catching, or clicking, otherwise the same as Group A. In Group C the findings were indefinite—swelling, pain, disability, in Group D the findings were misleading, and in Group E the clinical data were inadequate (8.5 per cent of the cases).

It is to be noted that an accurate diagnosis is usually not so readily made on clinical grounds alone, without radiographic assistance, and frequently is limited to "internal derangement."

The accuracy of the clinical examination alone is indicated by the following percentages: Group A, 47.7 per cent, Group B, 23.7 per cent, Group C, 5.8 per cent, Group D, 14.3 per cent. The total for Groups A and B was 71.4 per cent and for Groups C and D 20.1 per cent. This is exclusive of the 8.5 per cent for which the clinical data were inadequate. The percentages for the first two-year interval and the third year agree very closely.

Accuracy of Clinical Examination and Pneumoarthrogram Considered Together (Table VI). For this analysis the cases are divided into the following groups: Group 1, in which both the clinical diag-

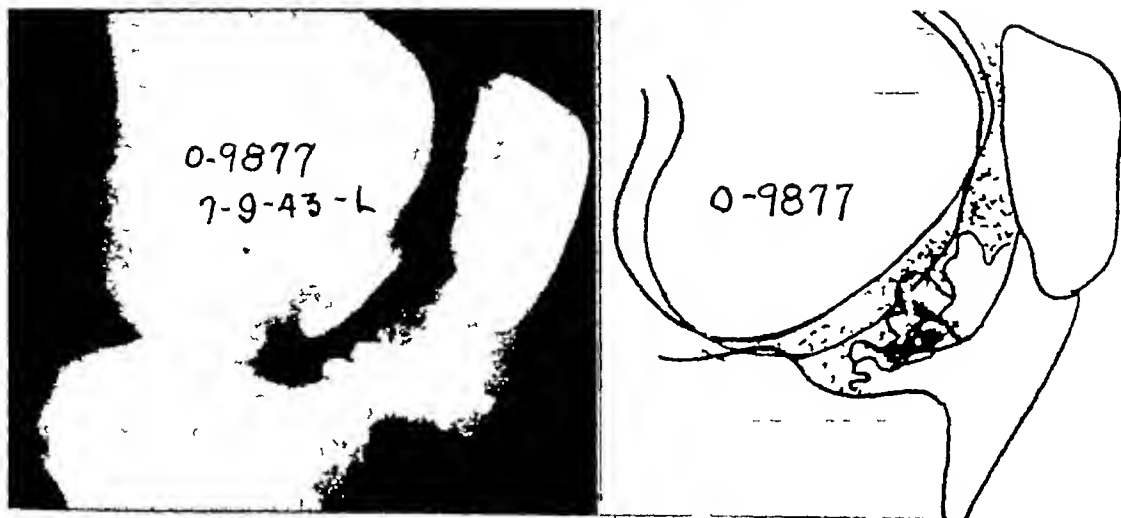


Fig 29 Hypertrophied and hemorrhagic fat pads—filling up usually seen infrapatellar clear space

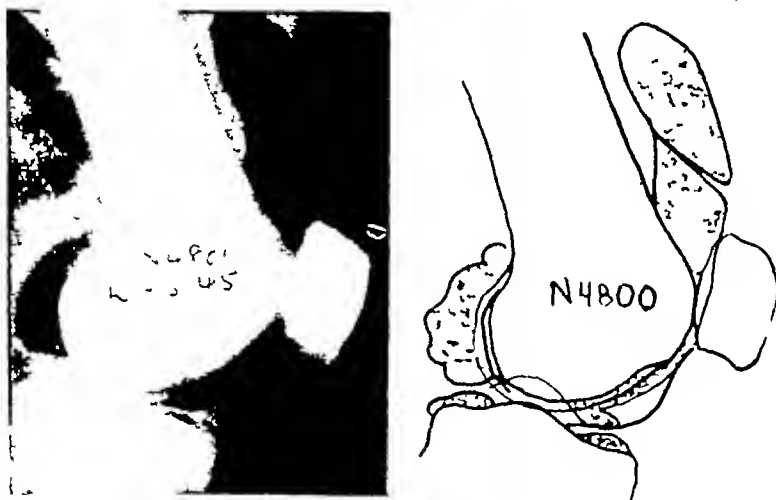


Fig 30 Fat pad adherent to the tibial plateau

nosis and the pneumoarthrograms were accurate, Group 2, in which both were inaccurate, Group 3, in which the pneumoarthrograms were entirely or partially correct while the clinical diagnosis was misleading, Group 4, in which the clinical diagnosis was accurate but the pneumoarthrograms were misleading or erroneous or unsatisfactory, Group 5, in which the pneumoarthrograms were either entirely or partially correct, but the clinical data were inadequate

The pneumoarthrograms and the clinical diagnosis were equally accurate in 41.7 per cent of the cases seen in the first two-year

interval, and 63.2 per cent in the third year, an over-all percentage of 47.4 per cent. The diagnoses were equally erroneous in 6.2 per cent during the first two years and 6.9 per cent in the third year, an over-all percentage of 6.4 per cent. The clinical diagnosis was accurate where the pneumoarthrograms were not in 28.1 per cent in the first two-year interval, and in 11.5 per cent in the third year, an over-all percentage of 23.7 per cent. The reverse was true (i.e., the clinical diagnosis was inaccurate and the pneumoarthrograms accurate) in 15.3 per cent during the first two years, and 10.3 per cent in the third year, an over-all

TABLE VII ANALYSIS OF ERRORS

Type of Error	Medial Meniscus	Lateral Meniscus	Total
Errors of commission	15	8	23
April 1942-44	(8)	(5)	
April 1944-45	(7)	(3)	
Errors of omission	33	10	43
April 1942-44	(30)	(7)	
April 1944-45	(3)	(3)	
TOTAL	48	18	66*

* Wrong side diagnosed in two cases

TABLE VIII MAJOR ERRORS

Type of Error	April 1942-44	April 1944-45	Total
Errors with osteochondritis	4	5	9
Anomalously short meniscus considered bucket-handle fracture	1	3	4
Tip fracture (cornua) not shown on films	15	0	15
Medial meniscus	(13)		
Lateral meniscus	(2)		
TOTAL	20	8	28

figure of 14 per cent. It is very significant that in the third year either the clinical diagnosis or the pneumoarthrogram was of value where the other was not in approximately an equal number of cases, and in addition, the pneumoarthrogram was of value in 8 per cent of the cases where clinical data were inadequate for analysis.

Analysis of Errors in Diagnosis (Tables VII and VIII) There were a total of 66 errors in 64 cases, the duplication occurring where the lesion was diagnosed on the wrong side, thus involving both an error of commission and omission. There were 23 errors of commission, 15 in the medial meniscus and 8 in the lateral. There was no significant difference in this group between errors made in the third year and in the first two-year period. There were 43 errors of omission, 33 involving the medial and 10 the lateral meniscus. In this case the difference between the first two-year interval and the third year is significant. There were 30 errors of omission with regard to the medial meniscus in the initial two-year period, whereas there were only 3 in the third.

In the third year there were 10 errors of commission, and 6 of omission, whereas in the first two-year period there were 13



Fig 31 Obliterated suprapatellar bursa as the result of previous injury. Note the healed fractures of the patella.

errors of commission and 37 of omission. Considering these results in the light of 230 examinations in the first two-year interval as against 85 in the third year, there was an over-all improvement in accuracy in the third year, but the relative numbers of errors of commission actually increased in the third year. The great improvement came in avoiding errors of omission.

For the entire three-year period, 48 of the errors involved the medial meniscus, and 18 the lateral. This gives approximately the same ratio for errors as for the incidence of lesions at the two sites. In the first two years 38 errors involved the medial and 12 the lateral meniscus, whereas in the third year 10 involved the medial and 6 the lateral.

Approximately 23 per cent of all errors were due to cornu fractures of a meniscus which were not shown on the films. All of these errors were made in the first two-year period, and all but two of them were in relation to the medial meniscus. Approximately 14 per cent of all of the errors were in cases which also had osteochondritis of one type or another. It has been our experience that confusing air shadows are not infrequent in cases of osteochondritis dissecans. An anomalously short meniscus simulating the bucket-handle type of fracture caused four of the errors, but fortunately this is an unusual occurrence.



Fig 32 Synovium The sharply demarcated tumor is seen projecting into the shadow of the supra patellar bursa

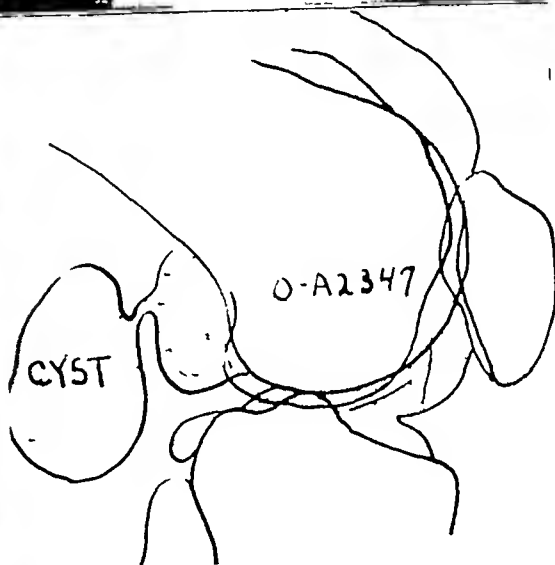
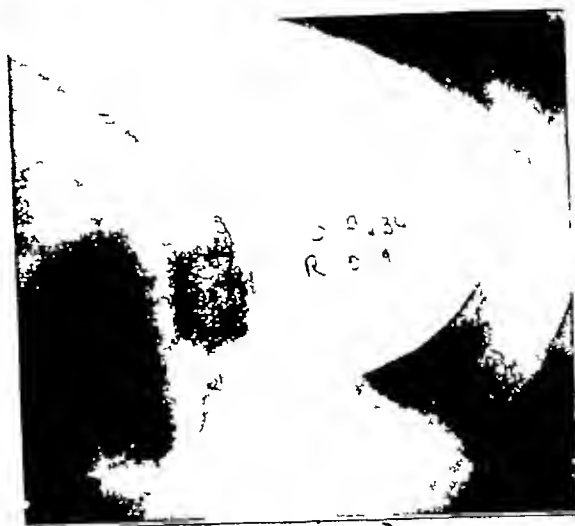


Fig 33 Popliteal cyst (bursa) The communication between the posterior pouch and the cyst is well visualized

approximately 2 to 5 and together account for two-thirds of the major lesions in internal derangements of the knee joint

GENERAL ANALYSIS OF STATISTICS

Abnormalities of the lateral meniscus and medial meniscus are found in a ratio of

about one-third of the cases. In a few of these the fat pad was torn, or loose bits were free in the joint, or the pad was adherent to one of the cartilaginous structures. In these few cases abnormality of the fat pad can probably truly be called a major pathologic change. Otherwise, fat pad abnormalities are usually secondary to some other pathologic process in the joint.

About one-quarter of the patients had

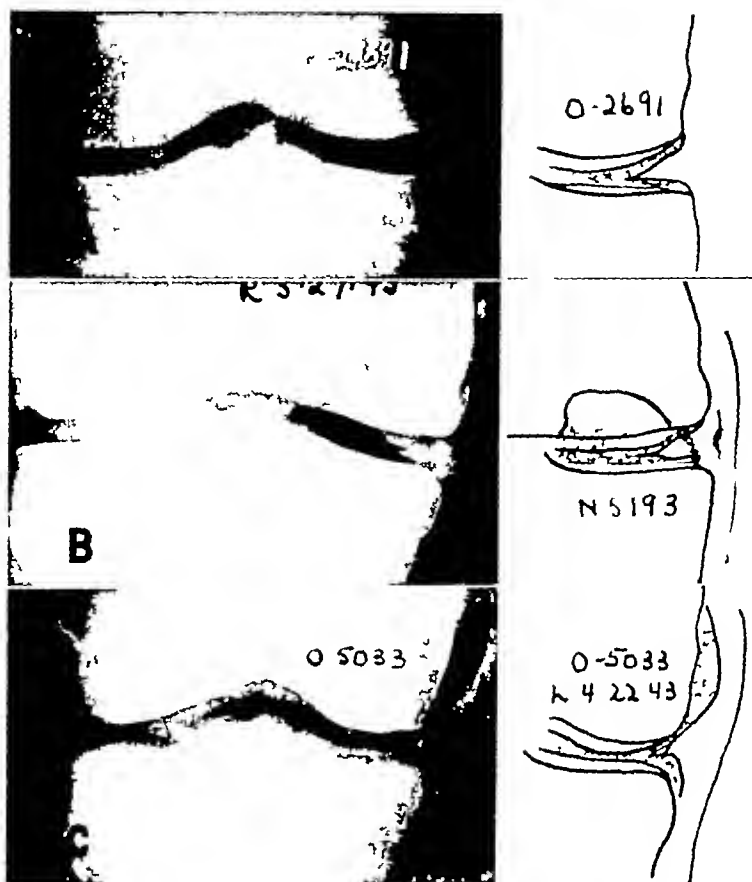


Fig 34 Analysis of erroneous diagnoses A Fractured anterior or posterior cornua not indicated on the films B Osteochondritis dissecans with unusual extraneous shadows superimposed over the meniscus C Anomalously short meniscus otherwise normal simulating an absent meniscus or dislocation tear of the meniscus (bucket handle fracture)

either osteochondritis dissecans or chondrosis of the patella. This frequency is approximately one-half that of medial meniscus lesions, and 5 per cent greater than the incidence of abnormalities of the lateral meniscus. About one-quarter of the cases with osteochondritis or chondrosis also had loose bodies in the joint, in about one-half there were other major pathologic changes in the knee joint, such as a fractured meniscus. The relatively high incidence of chondrosis of the patella is noteworthy. Its frequency was almost equal to that of osteochondritis of the medial femoral condyle alone, and it was not infrequently associated with a loose body. Plain radiographs of the knee are probably just as

valuable as pneumoarthrograms in the diagnosis of this abnormality.

Cornu fractures of a meniscus, especially the medial, are very difficult to diagnose and may escape detection. These accounted for approximately one-quarter of all our errors of the past three years. Many of the errors of omission of the first two-year interval have now been corrected with improved technic. Actually errors of commission are now the greater problem, whereas previously the reverse was true.

Our greatest improvement in diagnosis in the past three years has been in taking pneumoarthrographic studies out of the unsatisfactory group from a technical standpoint (Group C) and placing these in

a diagnostic group The relative percentage of errors has diminished only from 20.7 to 16.1 per cent

In its present stage of development, the pneumoarthrogram is approximately 80 per cent accurate We believe that the clinical examination at best is approximately 70 per cent accurate Thus *the pneumoarthrogram has achieved a greater accuracy than the clinical examination* Moreover, in the case of the pneumoarthrogram, the type and completeness of the lesion can be more accurately predicted This more complete information is especially valuable when both the medial and the lateral menisci are involved in the same knee Both abnormalities can thereafter be corrected at the same time, a condition not very likely without the assistance of pneumoarthrography

It is also highly significant that the pneumoarthrogram and clinical examination are frequently complementary and permit a greater accuracy when employed together Frequently, the pneumoarthrogram is accurate where the clinical examination is not, and *vice versa*, so that *when one arrives at a diagnosis both clinically and radiographically, a very high degree of accuracy is achieved, probably in the neighborhood of 90 per cent* As in all phases of diagnostic medicine, the clinical and the radiographic pictures must ultimately be viewed together in order to obtain the most accurate diagnosis

SUMMARY

1 A technic for pneumoarthrography of the knee, employing a special device for spreading the knee joint, is described

2 The normal pneumoarthrogram is discussed, and its various normal appearances are illustrated

3 The abnormal pneumoarthrogram is discussed, and its various pathological appearances are illustrated

4 The pneumoarthrogram is of special value in the diagnosis of abnormal menisci, fat pads, and bursae These cases account for over two-thirds of the major lesions in internal derangements of the knee joint

5 In other causes of internal derangement of the knee, the plain radiographs are usually of equal value for diagnosis Oxygen contrast is not as a rule necessary for the diagnosis of osteochondritis dissecans or chondrosis of the patella

6 Popliteal bursae are probably seldom of pathologic significance They occurred in 13.5 per cent of the present series

7 The pneumoarthrogram was found to be 81.6 per cent accurate It is estimated that the clinical examination alone is about 70 per cent accurate, and frequently the exact nature of the lesion cannot be diagnosed The pneumoarthrogram has thus proved its value as an excellent diagnostic measure When the pneumoarthrogram and the clinical examination are considered together, it is found that they are equally good in 47.4 per cent of the cases, and supplement one another in 37.7 per cent of the cases With their combined use, a 90 per cent accuracy can probably be achieved

8 The errors made have been analyzed and compared for the first two years of this three-year study and the third year In the third year the percentage of erroneous diagnoses diminished from 20.7 per cent to 16.1 per cent The greatest improvement was made in reducing the unsatisfactory examinations and partially correct examinations from 24 per cent to 6.9 per cent, thus increasing the percentage of accurate diagnoses from 55.3 per cent to 77 per cent

9 We have found pneumoarthrography of the knee joint to be without risk and now practice it routinely in all cases of suspected internal derangement

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SUMARIO

Nueva Neumoartrografía de la Rodilla con su Valuación en 315 Casos

La técnica descrita utiliza para la neumoartrografía un artefacto especial que distiende la rodilla. El tobillo y el muslo se colocan en fayas o abrazaderas, moviéndose el primero hacia un lado y luego hacia el medio en un bloque de madera colocado a lo largo del punto de origen lateral o medial de la articulación, lo cual ensancha el espacio articular del lado opuesto del bloque en turno para las distintas exposiciones. Cuando las películas corrientes en las posiciones dorsal y prona no facilitan una visualización suficientemente exacta de los meniscos, se voltea la rodilla para un lado u otro, dejando que se eleve el oxígeno inyectado, se extiende la rodilla sobre un bloque que sirve de punto de apoyo, y se asienta el haz de rayos X horizontalmente a través de la articulación. Los grabados y diagramas adjuntos revelan los hallazgos normales y anormales en los varios tejidos de la rodilla.

Este procedimiento ha sido empleado en

315 casos operados subsiguientemente y en los que se basa la comunicación actual.

El neumoartrograma resultó de valor decidido en el diagnóstico de anomalías de los meniscos, acumulaciones de tejido adiposo y bolsas, que comprenden más de dos terceras partes de las grandes lesiones en los trastornos internos de la rodilla. En los debidos a otras causas, las películas corrientes suelen resultar de igual valor diagnóstico. Por regla general, no se necesita el contraste con oxígeno para el diagnóstico de la osteocondritis disecante o condrosis de la rótula. Pueden descubrirse también las bolsas poplíteas, pero probablemente rara vez poseen importancia patológica.

En la serie descrita, las neumoartrografías mostraron una exactitud aproximada de 80 por ciento, comparado con 70 por ciento para los estudios clínicos aunque los últimos frecuentemente no revelaron la naturaleza exacta de la lesión. Las dos

clases de examen resultaron igualmente buenas en 47.4 por ciento de la serie y se complementaron mutuamente en 37.7 por ciento, en tanto que, combinadas, alcanzaron una exactitud de 90 por ciento.

El porcentaje de errores radiológicos en el diagnóstico bajó de 20.7 en los primeros dos años en este estudio trienal a 16.1 en el

tercer año. El mayor adelanto consistió en rebajar la proporción de exámenes poco satisfactorios y parcialmente correctos de 24 por ciento a 6.9 por ciento, haciendo subir así el porcentaje de diagnósticos exactos de 55.3 a 77.

No se han observado complicaciones con el procedimiento, el cual parece inocuo.



Dissecting (Intramural) Pharyngo-Esophageal Diverticulum¹

ABRAHAM MELAMED, M.D.,² and LYNN J. WALKER, M.D.

Milwaukee, Wis

A DISSECTING pharyngo-esophageal diverticulum has, to the best of our knowledge, never been reported in the literature. The roentgen signs of such a dissecting form of pulsion diverticulum are characteristic and permit of a preoperative diagnosis, once the pathological possibility of such a lesion is established.

The intramural pharyngo-esophageal diverticulum in the case to be recorded here was situated posteriorly between the mucosa and muscularis of the esophagus. The roentgen appearance and characteristics of such a lesion can quite readily be surmised. Although there are points of similarity between the intramural and extramural forms, one can easily differentiate one from the other. It is hoped that the description of our findings will lead to the discovery of more such forms of pharyngo-esophageal diverticulum before surgical extirpation is attempted. Our patient would have been spared some anxious and dangerous moments had the roentgen features been fully appreciated and a correct preoperative diagnosis been made.

CASE REPORT

R. K., a boy of 15, in September 1945 told his step father, a physician, that he had been having difficulty in swallowing for about one month. He encountered more difficulty with solid foods than with semisolids or fluids. With the latter two, repeated swallowing would serve to relieve the discomfort but meat and similar solids would 'get caught' and it would be necessary to 'cough them up' before relief was obtained. The patient noticed no swelling of the neck following the intake of food fluid or solid. He had lost no weight.

For years the patient had been in the habit of swallowing his food after very little mastication. He had had mumps and measles during early childhood. His father died at the age of thirty-nine after

a 'heart attack'. His mother is living and well, except for attacks of migraine headaches. There are no brothers or sisters.

The patient was tall and thin, 6 feet 2 inches in height and weighing approximately 165 lb. Examination of the head was essentially negative. The neck was extremely long but no swelling or lymph adenopathy was found. No abnormalities were discovered in the chest, abdomen, or extremities.

The blood Wassermann test was reported as negative. The red blood cell count was 5,100,000, the white blood cell count 8,200, with a normal differential count. The sedimentation rate was normal and urinalysis disclosed no abnormalities.

Roentgen examination of the upper gastrointestinal tract with the aid of a barium meal on Sept. 29, 1945, disclosed a diverticulum in the lower cervical region. No obstruction or dilatation was observed. The diverticulum arose at about the level of the 6th or 7th cervical vertebra, was situated posteriorly, and could not be separated from the esophagus proper at any time during examination. After the ingestion of approximately half a glass of barium mixture the diverticulum attained a size of approximately 2 x 5 cm (Fig. 1). A sphincter-like configuration of the diverticular neck was observed (arrow). There was a peculiar 'lifting' of the diverticulum when the patient was asked to swallow without further administration of the barium sulfate mixture, and with every such swallow, whether he was in the upright or recumbent position, the diverticulum diminished in size. After several such 'blank' swallows it measured no more than 1.5 cm in diameter (Fig. 2). The diverticulum was 'lost' in the lateral view (Fig. 3). A close relationship between the barium-filled esophagus and diverticulum was maintained in the anteroposterior and oblique positions but in the lateral view the diverticulum seemed to disappear. The roentgen diagnosis was pharyngo-esophageal diverticulum, but the unusual features described above could not be accounted for satisfactorily. It was thought possible that the diverticulum was situated slightly to one side of the mid line and therefore overlapped the opacified esophagus in the lateral view. The 'contraction' phenomenon was to say the least, puzzling. The only explanation offered was that the capacity of the diverticulum might have been limited by the close approximation of the cervical structures in the boy's long narrow neck.

¹ From the Department of Radiology, Evangelical Deaconess Hospital, Milwaukee, Wis. Accepted for publication in January 1947.

² Director, Department of Radiology, Evangelical Deaconess Hospital, Milwaukee, Wis.



Fig 1 Right anterior oblique projection of pharyngo-esophageal diverticulum opacified immediately after swallowing 4 ounces of a barium mixture. The diverticulum never attained a size larger than 2×5 cm. Note sphincter like outline (arrow) at the origin of the diverticulum

The patient was taken to the Mayo Clinic, where the diagnosis of pharyngo-esophageal diverticulum was confirmed and surgery was performed on June 13, 1946. The surgical findings and pathological findings as submitted by Dr. Howard K. Gray are as follows:

"Exposure through an incision which was made along the posterior border of the sternocleidomastoid on the left revealed a very deeply situated esophagus. There was almost complete mobilization of the esophagus well into the mediastinum and there was no evidence of an extra-esophageal diverticulum. A longitudinal incision was made in the left lateral wall of the esophagus approximately 6-7 cm. in length, and on the posterior wall of the esophagus just opposite the cricoid level was an esophageal pouch which emptied readily, admitting the index finger and extending for approximately 2.5 to 3 cm. posteriorly under the muscularis. This mucosal pouch was turned inside out and excised, suturing the base of the pouch with one continuous suture of silk. The longitudinal opening in the esophagus was then closed with multiple interrupted sutures of silk and reinforced by attempts to patch over this area the remaining portion of the muscularis. In order to obtain exposure the sternocleidomastoid muscle was cut in its mid portion and in closing, the two ends of this muscle were brought together with mul-

tiple interrupted mattress sutures of chromic catgut. Two Penrose drains were left in the wound, one down into the mediastinum and one up to the margin of the opening in the esophagus. A Rehmann tube was placed in the stomach at the time of the operation and should be left in place for at least a week.

"The pathologists reported a pharyngo-esophageal diverticulum."

Course Following surgery, several serious complications arose. A marked degree of tracheal obstruction, due to edema, developed secondary to the



Fig 2 Reduction in size of diverticulum after 'blank' swallowing, patient still in upright position

extensive resection. An emergency tracheotomy was performed one day following the operation. Soon afterward collapse of the right lung occurred. Thereafter, with active symptomatic treatment the patient made an uneventful recovery.

Follow-up Record Postoperative roentgen examination of the esophagus at the Mayo Clinic revealed no abnormality in the pharyngo-esophageal area, and the patient was dismissed approximately five and a half weeks following admission. Before his discharge plastic repair of the cervical and tracheotomy wounds was performed. Keloid formation in the operative and tracheotomy scars was subjected to superficial x-ray therapy with excellent results.

COMMENT

Diverticula of the esophagus are usually described as either of pulsion or traction



Fig 3 Lateral projection of barium-filled esophagus and diverticulum during the act of swallowing. Note superimposition of the opacified diverticulum and esophagus proper. The piriform shadow of greater density (outlined by arrows) represents the filled intramural diverticulum.

type, but Templeton (5) considers a third class, namely, functional diverticula. On the basis of our experience, we have subdivided the pharyngo-esophageal pulsion diverticula into two categories: (1) intramural or dissecting, (2) extramural or extra-esophageal. The classification is as follows:

- I Functional diverticula
- II Traction diverticula
- III Pulsion diverticula
 - A Pharyngo-esophageal
 - 1 Extra-esophageal or extramural
 - 2 Dissecting or intramural
 - B Supradiaphragmatic or "epiphrenic"

It is beyond the scope of this paper to consider in detail the pulsion and traction types of esophageal diverticula. They are discussed by many authors, including Kulvin (1), Lahey (2), Melamed and Zimmerman (3), Pancoast *et al* (4), and Templeton (5). It will suffice to recall a few established facts as to pharyngo-

esophageal diverticula. These diverticula arise at about the level of the 6th cervical vertebra below the level of the cricoid cartilage. The outer muscular layer of the esophagus consists of longitudinal fibers, while the inner layer is comprised of circular fibers. Herniation of pharyngo-esophageal diverticula ordinarily occurs through a V-shaped gap posteriorly, where the longitudinal fibers divide at the cephalad end of the esophagus. These diverticula, for unexplained reasons, are seen most frequently on the left side (1, 4).

Pharyngo-esophageal diverticula occur chiefly in middle-aged persons, and symptoms have usually been present for many years before medical advice is sought. Our patient was unusually young, probably one of the youngest on record. The etiology of the dissecting form of pharyngo-esophageal diverticulum which he displayed has not been ascertained, but the evidence seems to point to a developmental abnormality. Probably a sac or fold was present from birth and was slowly enlarged and/or opened when traumatized by unusually large boluses of food. From the time of onset of symptoms to the time of surgery—a period of ten months—the symptoms were identical and did not increase in severity. Nor was there any appreciable change in the size and shape of the diverticulum during the interval between roentgen examinations—approximately nine months. At the time of surgery it was impossible to demonstrate any thinning of the wall of the diverticulum at any one point.

Previous mention in this paper has been made of the tendency of the diverticulum to empty after repeated "blank" swallowing. The reason for this is quite evident when one realizes that the sac lay entirely inside the muscular layer. It is purely conjectural to envisage what might have occurred had the patient been allowed to go untreated for a number of years. Would the diverticulum have remained stationary in size? Would it have increased in size by dissecting further between the mucosal and muscular layers, or would it eventually

have herniated through the muscular wall posteriorly and assumed the usual appearance of a pharyngo-esophageal diverticulum? Does the dissecting type of diverticulum represent an "aborted" form of the ordinary pharyngo-esophageal diverticulum, the momentarily weakened muscular wall having regained its integrity, forcing the sac down between the mucosa and muscularis instead of leading to posterior herniation? These questions are left unanswered pending the discovery of more such cases, more pertinent etiological facts, common denominators, etc

The requirements and details of complete roentgen examination of the esophagus have been reviewed by Templeton (5), Melamed and Zimmerman (3), and others. In our case the roentgen signs were identical whether the patient was examined in the upright or recumbent position. In the light of the established pathology and conception of pharyngo-esophageal diverticula, the observation of emptying of the diverticulum with the patient upright was most disturbing and incomprehensible. The contraction of the esophagus around the diverticulum actually expressed the contents of the sac, thereby reducing the size of the diverticulum. The diverticulum appeared to rise or be "lifted" during deglutition due to evacuation, the contracting esophagus expelling the contents of the intramural sac. The extramural type contains no muscular tissue, is incapable of contraction, and empties only when the patient is placed in a position in which the fundus of the diverticulum is brought above the level of the diverticular neck. Such extra-esophageal diverticula become distended while the patient is in the upright position and are usually larger than the one in our patient. The extramural form usually occurs on the left side (1, 4). The intramural diverticulum in our patient occurred in the mid-line posteriorly, and a sphincter-like configuration of the diverticular neck (Fig 1) was noted. In retrospect, on close inspection of the lateral projection, a piriform shadow of relatively greater density (arrows) than the barium-

filled esophagus proper can be found. Very close scrutiny of the lateral projection is mandatory in every case of pharyngo-esophageal diverticulum.

SUMMARY

A dissecting form of pharyngo-esophageal diverticulum is described in a 15-year-old boy. Symptoms were present for only one month prior to the first roentgen examination and surgical extirpation was performed nine months later.

The roentgen signs of the intramural pharyngo-esophageal diverticulum in this patient were as follows: (1) opacification and emptying of the diverticulum during examination in the upright position, (2) an apparent elevation or "lifting" of the diverticulum during deglutition, due to expulsion of its contents by the surrounding and contracting esophageal musculature, (3) origin in the mid-line posteriorly, (4) obscuration or "disappearance" of the opacified diverticulum in the lateral view, due to superimposition of the opaque shadows of the diverticulum and esophagus proper.

If all dissecting pharyngo-esophageal diverticula occur in the mid-line posteriorly, one can easily appreciate the indispensability of the lateral view of the opacified esophagus and diverticulum in order to reveal the location of the pouch. Close scrutiny and careful analysis of the relative densities on the lateral esophagram are necessary if one is to determine the true nature of the diverticulum—either intramural or extramural.

425 E Wisconsin Ave
Milwaukee 2, Wis

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SUMARIO

Divertículo Faringo-Esofágico Disecante Intramural

Descríbese un divertículo faringo-esofágico disecante en un niño de 15 años. Sólo había habido síntomas desde un mes antes del primer examen roentgenológico y la extirpación quirúrgica se realizó nueve meses después.

En este paciente los signos radiológicos fueron los siguientes: (1) opacidad y vaciamiento del divertículo durante la deglución, (2) "elevación" del diafragma durante la deglución con disminución de tamaño del divertículo después de contraerse el esófago alrededor del saco, (3) origen detrás de la línea media, (4) oscurecimiento o

"desaparición" del divertículo "opacificado" en la vista lateral, debido a la superposición de las sombras opacas del divertículo y el esófago mismo.

Si todos los divertículos faringo-esofágicos disecantes se presentan detrás de la línea media, es fácil apreciar cuán indispensable es la vista lateral del esófago y el divertículo oscurecidos para revelar la localización de la bolsa. Para determinar la verdadera naturaleza—ya intra- o extra-mural—del divertículo hay que escudriñar y analizar con cuidado las densidades relativas en el esofagrama lateral.



Spinal Extradural Hemangioblastoma Roentgenographically Visualized with Diodrast at Operation and Successfully Removed¹

I M TARLOV, M D

Brooklyn, N Y

EXTRADURAL hemangioblastomas of the spine appear to be relatively uncommon. Four instances of intraspinal hemangioblastoma were recorded by Elsberg (1) in a series of 253 intraspinal tumors, and but one of these was extradural. So-called hemangiomas of the vertebrae resulting in cord compression are more common. In 1943 Blackford (2) collected 65 such cases from the literature, including one of his own. On the basis of his microscopic description of the tumor, Blackford's case, and probably some of the others as well, were most likely hemangioblastomas, that is, true neoplasms composed of growing angioblasts rather than hemangiomas (angiomas), which are vascular malformations. This distinction has been clearly made by Cushing and Bailey (3), although considerable confusion of terminology still exists with respect to these lesions.

It is the purpose of this communication to relate an experience which, so far as is known to the writer, is unique. A pulsating hemangioblastoma arising from the spinal extradural space was encountered. At the time of the first operation the extent and the true nature of the lesion were not apparent, and it was considered inoperable. At a second operation, diodrast was injected into the mass and its extent as well as its main vessels of supply and drainage were clearly portrayed. It was then possible to extirpate the tumor and bring about functional recovery.

CASE REPORT

History. H N, a 42 year old male, entered the Hospital June 15, 1946, complaining of numbness

and coldness of the feet as well as weakness of the lower extremities of fifteen years' duration, urgency and frequency of urination with diminution of sexual potency for two years, occasional low back pain with radiation down the entire left lower limb. The symptoms were progressive.

Examination. The general physical examination revealed a hard, freely movable mass, unattached to the skin, measuring 3.5×5.0 cm, located in the right anterior superior cervical triangle. The mass had first been noticed three years earlier and had increased in size gradually. A similar mass excised from the left cervical region sixteen years previously was diagnosed "tuberculous adenitis" on microscopic examination. The only other abnormal finding on general examination was the presence of hypertension (240/150). Neurological examination revealed the following abnormal findings: moderate weakness of both lower limbs, greater on the left, very active knee and ankle jerks with bilateral ankle clonus, absence of cremasteric reflexes, and bilateral extensor plantar responses, impairment in appreciation of pin-prick, hot and cold objects, and cotton-wool below the level of the groin on both sides, with a slight degree of sacral sparing of sensation, absence of appreciation of position sense of the great toes and vibration at the ankles.

X-ray examination of the thoracolumbar spine revealed a destructive process involving the pedicles and laminae of the eleventh and twelfth vertebrae on the left side (Fig. 1). There was also a spotty increase of density involving the posterior aspect of the body of the eleventh thoracic vertebra. Lumbar puncture with manometric study (Grant-Cone method of graduated jugular compression with a blood-pressure cuff) revealed evidence of a complete subarachnoid spinal block. The cerebrospinal fluid contained no cells and showed a negative Pandy reaction, the total protein content had not been determined. The Wassermann reaction of the cerebrospinal fluid was negative and the colloidal gold curve was normal. It seemed quite clear that the patient was suffering from a tumor involving the eleventh and twelfth thoracic vertebrae with compression of the spinal cord.

Further diagnostic studies were unnecessary but, due to a misunderstanding fluoroscopic examination

¹ From the Neuro-surgical Service of the Jewish Hospital of Brooklyn, New York. Accepted for publication in January, 1947.



Fig 1 A (left) Roentgenogram showing obliteration of pedicles of D11 and D12 on the left side B (right) Lateral view showing obscuration of posterior margins of the body of D11 and possibly of D12 with alteration in the density of the vertebrae

following the intraspinal (L5-S1) injection of 3 c.c. of pantopaque was done. Evidence of a spinal block at the upper border of the first lumbar vertebra was revealed. The pantopaque was removed immediately upon completion of the examination.

Operation Under general anesthesia a laminectomy (T11 and T12) was done on June 18, 1946. A large, smooth, reddish mass which pulsated vigorously, was found underlying the excised laminae and compressing the spinal cord severely (Fig 2A). Aspiration yielded blood and upon withdrawal of the needle there occurred brisk bleeding which, however, was readily controlled by a piece of crushed muscle. It was my impression that the mass represented a large aneurysm, and attempt at its removal was considered hazardous particularly in view of the marked degree of hypertension that existed. The wound was closed and it was hoped that some benefit would result from the decompression of the lesion.

Postoperative Course Steady loss of all function of the lower limbs occurred together with urinary retention, so that nine days after operation only very feeble movement of the limbs was possible and there was practically complete loss of all forms of sensory appreciation below the level of the twelfth thoracic dermatome bilaterally. In view of the downhill course, it was decided to re-explore the lesion and

attempt to visualize its extent by the use of diodrast as a prelude to possible removal.

Second Operation On June 27, 1946, the laminectomy wound was re-explored. The pulsatile mass was exposed and preparations were made for the injection of a 35 per cent solution of diodrast. A 20 gauge needle was introduced into the mass and bright red blood was aspirated, following which a total of 5 c.c. of diodrast was injected. After 3 c.c. of the solution had been introduced, postero anterior films of the spine were obtained with portable apparatus with Bucky diaphragm (Fig 3, A). A second injection of 5 c.c. of diodrast was carried out while lateral views were taken with the use of the L₁ sholm grid (Fig 3 B). Cassettes with fast screens were used. One second exposures were made at 15 ma 60 kv, with a target-film distance of 25 inches. Moderate resistance to the injection of the diodrast was encountered on each occasion.

The films obtained following the injection of diodrast into the mass clearly outlined the lesion and revealed a large blood vessel at its upper pole. It was still my impression that we were dealing with an aneurysm and preparations for an attempt at its removal were made. The left lateral wall of the vertebral canal at the level of D11 and D12 was removed by means of chisel and mallet and the large

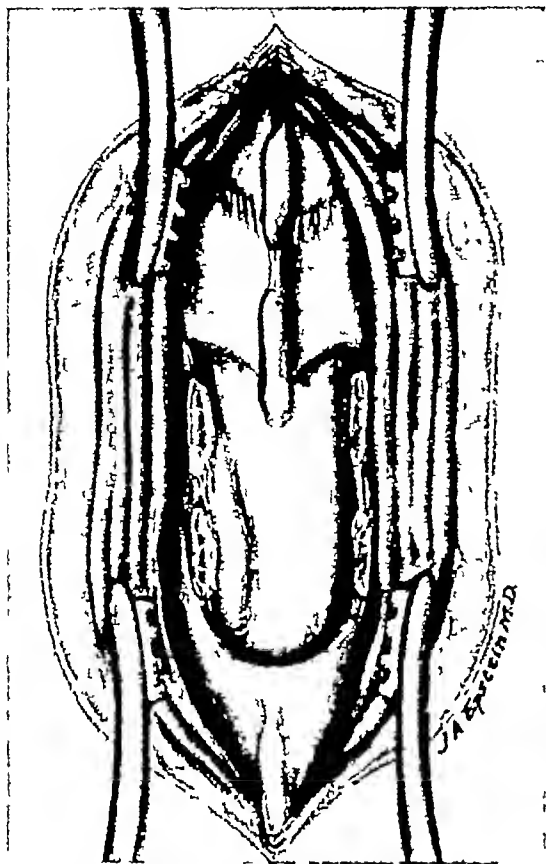


Fig 2A Drawing showing compression of spinal cord by the tumor which partially underlay it

vessels entering its superior pole were doubly ligated and severed between silver clips, following which pulsation of the mass ceased. The superior pole of the tumor was freed and the mesial aspect was then readily separated from the dura, to which it was only slightly adherent. The encapsulated mass was found to be quite adherent on its undersurface to the body of the eleventh thoracic vertebra. After their separation the body presented a raw porous bleeding surface (Fig 2B) and the contiguous surface of the tumor was ragged suggesting extension of the tumor into the body of the vertebra as indicated by the roentgenogram. Several large vessels in aggregate about 3 mm in diameter and approximately equal in caliber to the superior polar vessels, were clipped and cut as they entered the mass at its lower pole. The bleeding from the posterior surface of the body of D11 was controlled with bone wax. The wound was closed. The patient received a transfusion of 300 cc of blood on the operating table and his condition remained good throughout the procedure.

Subsequent Course. The patient showed a striking degree of improvement following removal of the tumor. He received a course of deep roentgen

therapy to the operative site, totaling 1,800 r. Nineteen days after the tumor was extirpated, power in the lower limbs was normal except for impairment in strength at the left knee, approximating 20 per cent. Bilateral ankle clonus and extensor plantar responses, however, persisted and the cremasteric reflexes remained absent. Sensation was normal

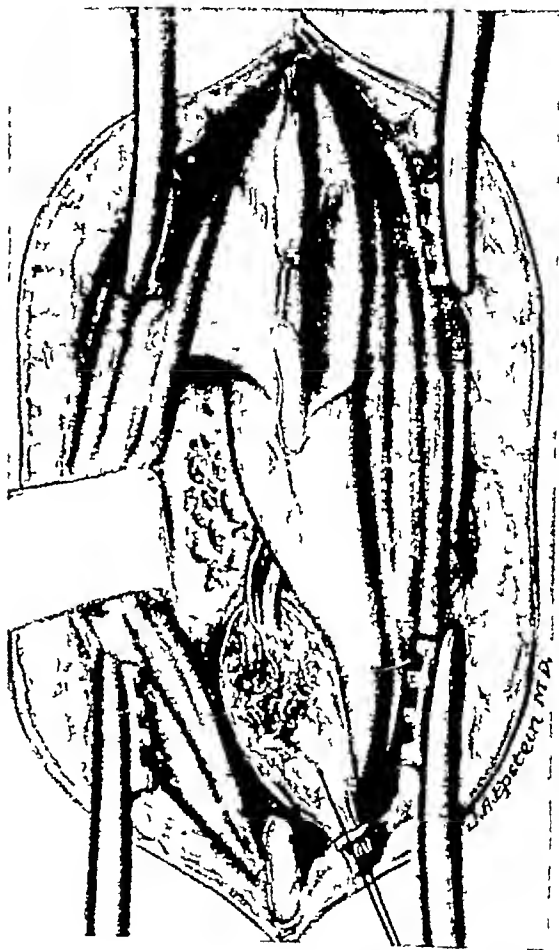


Fig 2B Drawing showing tumor in the process of removal. The superior vessels have been clipped and the vessels at the lower pole are shown. The porosity of the underlying bone, into which the tumor extended, can be seen.

except for pin prick and cotton wool appreciation over the anterior aspects of the thighs, which was said to be "nearly but not quite normal."

When the patient was seen on Aug 20, two months after operation, he had full motor power of the lower limbs and the gait was normal. Bilateral ankle clonus and extensor plantar responses still persisted. Sensation was still 'not quite normal' over the anterior aspects of the thighs.

Pathologic Examination. The tumor measured 3.4 × 1.7 × 9.0 cm. It was moderately soft. The external surface was pink and smooth except for the

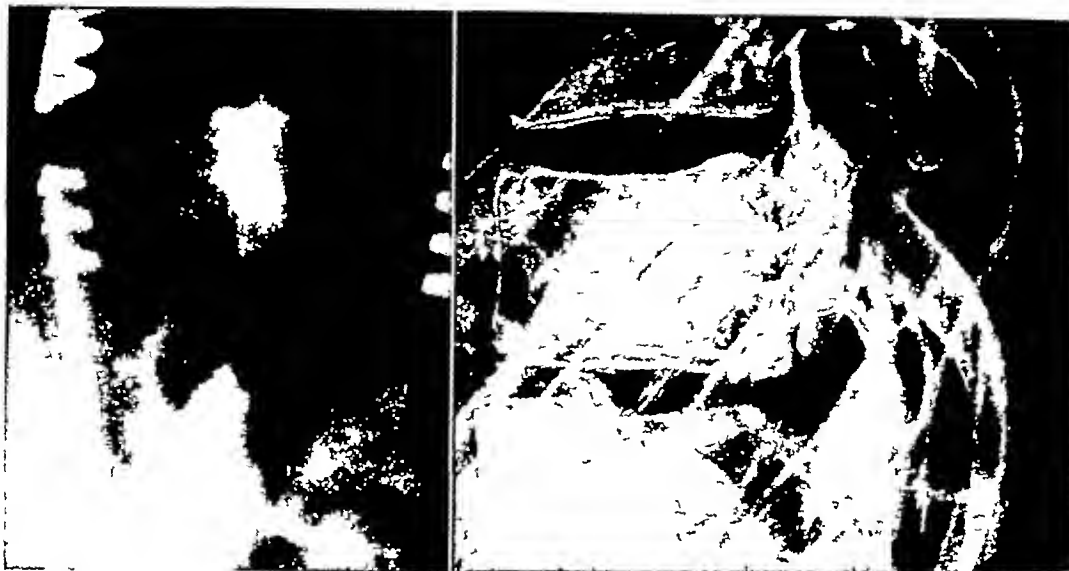


Fig 3 A (left) Roentgenogram showing the outline of the tumor after the injection of diodrast B (right) Sketch of lateral roentgenogram made following diodrast injection into the tumor The outline of the tumor, as well as the blood vessels at its upper and lower poles, is shown The original film was unfortunately lost

site of attachment to the body of the eleventh thoracic vertebra The cut surface (Fig 4) was red and rather spongy, and several large blood vessels coursed through it

The tumor was quite cellular, and its predominant feature was the presence of endothelial-lined channels many of which contained erythrocytes Some fully formed blood vessels with thick walls were seen, but most of the vessels were of the capillary and sinusoidal types (Fig 5) The cells lining the blood spaces varied from flat elongated cells to large cuboidal or polygonal cells containing vesicular nuclei These latter cells were identical with the type cell of the tumor Many of the tumor cells however contained nuclei of bizarre shape and some were multinucleated Mitotic figures were not encountered Some of the cells were vacuolated and resembled the so-called pseudo xanthoma cells also some hemosiderin laden phagocytes were seen In some areas there were invaginations of groups of large cells into the endothelial-lined canals In part these heaped up cells within the vessels possessed an endothelial cover, in addition, many large cells were present singly or in groups within the vessel lumen Throughout the tumor there was an abundant network of reticulin fibers which clearly outlined the numerous blood channels and merged with the abundant dense collagenous framework The base of the tumor at its zone of attachment to bone presented interdigitations of tumor cells and bone trabeculae

DISCUSSION

The hazards of attempting to remove spinal hemangioblastomas at operation

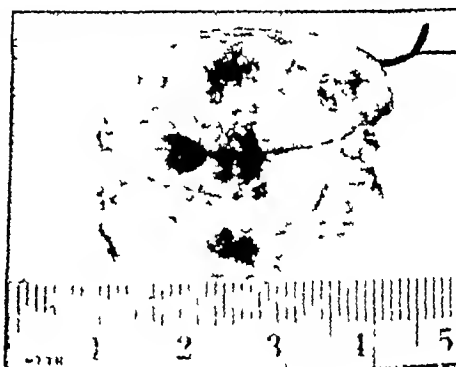


Fig 4 Cut surface of the tumor

have been stressed by various authors Blackford writes "Certainly surgery should not be attempted until roentgen therapy has failed or until paraplegia has developed" His attitude is the result of the high operative mortality associated with attempts at removal of these lesions (severe hemorrhage was frequent) and the fact that in 12 cases "cure" has been reported following the use of x-rays Blackford's own patient, an 18-year-old boy, was given roentgen therapy following biopsy and was in good health when last examined fourteen years after the onset of symptoms The cases collected by Blackford form a heterogeneous group, including both vascu-

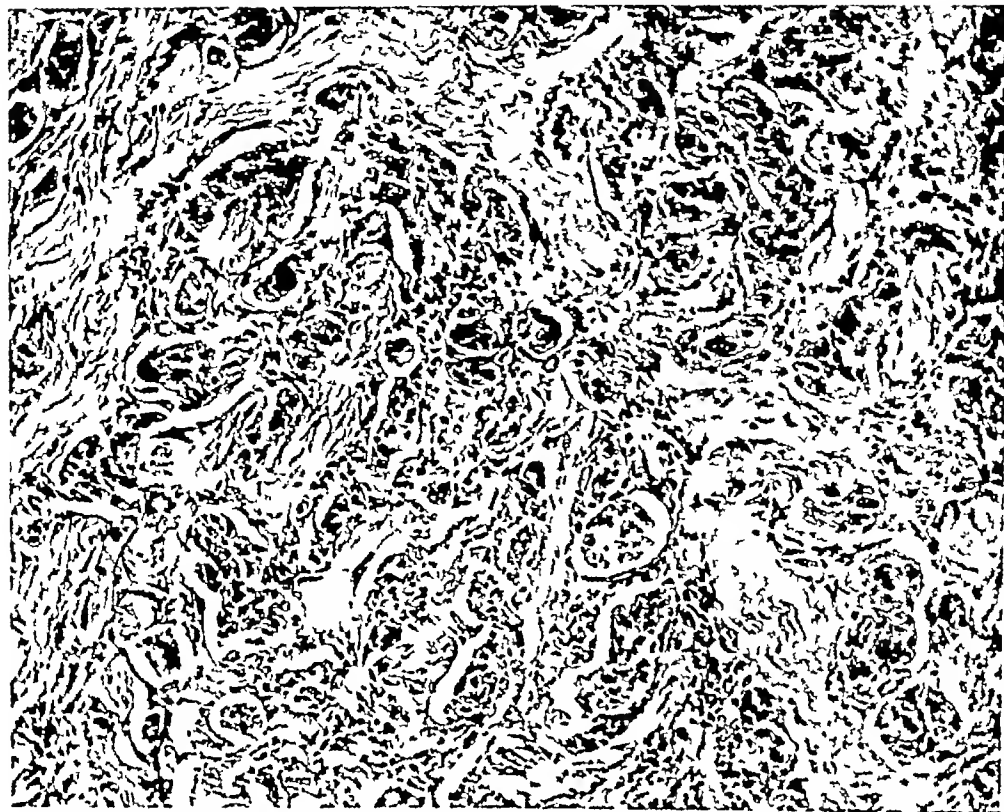


Fig 5 Photomicrograph of tumor showing numerous endothelial-lined channels, with invagination of tumor cells into the lumina of vessels. Hematoxylin and eosin $\times 150$

lar anomalies and neoplasms. It would be of interest to attempt a correlation of the precise histologic nature of the lesion with the clinical course following roentgen therapy, but the available data are insufficient for such a study.

Roentgen visualization of hemangioblastomas and angiomas after diodrast injection at operation would appear to render their removal safer. In this way the extent of the lesion together with the entering arteries and veins of exit might be readily determined. This was possible in the present case, in which the chief vascular supply of the tumor was interrupted as the initial step in its removal with the result that very little bleeding occurred thereafter. Blackford's wait-and-see policy appears unwise in cases where symptoms of marked spinal cord compression exist, since the hazard of irreversible spinal cord changes is too great.

The x-ray changes of the vertebrae in

the presence of hemangioma are considered to be characteristic, consisting in a sponge-like appearance or, more commonly, vertical striations, the result of thinning of the trabeculae of bone by the dilated cavernous spaces (4). This vertical striation was described in the case of Bailey and Bucy (5), which was successfully operated upon. The roentgen appearance of the hemangioblastoma in our case was unlike that seen in hemangioma, indicating, possibly, that these lesions may be differentiated radiographically.

The fact that the tumor reported here arose extradurally does not support the view of Globus (6) that hemangioblastomas ("pial (vascular) meningiomas of the hemangio-endotheliomatous type") arise from the pia mater. Nor does a leptomeningeal origin, as assumed for hemangioblastomas by Bailey, Cushing and Eisenhardt (7) and by Bailey and Bucy (8), seem likely, since the tumor was un-

attached to leptomeninges or dura mater. Many of these tumors bear a close resemblance to those described by general pathologists as hemangio-endotheliomas which arise from vascular endothelium anywhere in the body. Evidence of hemopoiesis within the tumor, such as has been reported in some cases of hemangioblastoma (3), was not seen in our case. The failure to demonstrate hemopoiesis in this tumor would seem to justify considering it as a hemangio-endothelioma. However, as Cushing and Bailey state, "this may be because of the difficulty of identifying such elements in ordinary microscopic preparations. We have unfortunately neglected to examine smears of fresh blood taken from these lesions at the time of operation." Evidence of blood cell formation in the tumor tissue alone would justify retention of the term hemangioblastoma rather than hemangio-endothelioma, which implies the formation of blood vessels rather than circulating blood elements from the tumor.

That the spaces within the tumor communicated with the general circulation is indicated by the fact that the diodrast was not visualized radiographically within the tumor after its removal at operation, the radiopaque material having entered the general circulation. It is likely that the frequent differences encountered between hemangioblastomas arising from the central nervous system and the hemangio-endotheliomas that arise elsewhere are attributable to environmental influences upon the tumor cells rather than significant differences in the cells of origin. In fact, many histological gradations between these various types of lesions occur.

SUMMARY

A case is reported in which the injection of diodrast at operation into an extradural spinal mass, at first thought to be an

aneurysm, afforded its roentgenographic visualization. As a result of the clear demonstration of the extent of the lesion, together with its entering arteries and veins of exit, it was possible to remove the mass surgically with but little bleeding. The tumor proved to be a hemangioblastoma. Following its removal there were complete return of motor power, previously impaired, and almost complete return of sensibility. It is concluded that this technic may prove useful in outlining the limits of some vascular lesions, including aneurysms of the brain and spinal cord, when encountered at the operating table. The extent of these lesions is not always apparent from their superficial appearance. Their visualization, with demonstration of their vascular supply by radiography with contrast dyes injected at operation, may aid in the decision as to whether surgical excision can be undertaken and facilitate their removal.

1150 Fifth Ave
New York 29, N Y

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SUMARIO

Visualización con Diodrasto de un Hemangioblastoma Raquídeo Extradural

Comuníquese un caso en el que la inyección de diodrasto al operar en una tumefacción raquídea extradural, tomada al principio por un aneurisma, permitió la visualización roentgenográfica. Gracias a la clara demostración de la extensión del tumor, así como de sus arterias de entrada y venas de salida, resultó posible extirparlo quirúrgicamente con muy poca hemorragia. La neoplasia resultó ser un hemangioblastoma. Después de excindirlo, se recuperó completamente la facultad motriz, anteriormente afectada, y casi completa-

mente la sensibilidad. Dedúcese que esta técnica puede resultar útil para delimitar los contornos de algunas lesiones vasculares, incluso aneurismas del cerebro y médula espinal, al dar con ellas en la mesa de operaciones, pues no se puede juzgar siempre la extensión de las mismas por su apariencia superficial. Su visualización, junto con la de su riego vascular, por medio de la radiografía con colorantes de contraste inyectados al operar, puede ayudar a decidir si la excisión resulta factible y facilitar la extirpación.

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Further Studies on the Relation Between Radiation Effects, Cell Viability, and Induced Resistance to Malignant Growth

IV Comparison of Effects of Roentgen Rays on Mammary Tumors Autogenous to Inbred Strains of Mice (dba and C3H)¹

ANNA GOLDFEDER, D Sc, M.U.C

New York, N Y

PREVIOUS PUBLICATIONS (1, 2, 3, 4) have reported the effects of λ -radiation experimentally determined on tumor cells *in vitro* and *in vivo*. Some of the results which emerged from these studies may be summarized briefly as follows

SUMMARY OF RESULTS WITH MOUSE SARCOMA 180

<i>Dosage Applied to Implants in vitro</i>	<i>Effects of Irradiation</i>
Up to 3000 r/air	Implants produced tumors in the hosts
From 3,500 to 4,000 r/air	Implants produced no tumors but rendered the animals immune to subsequent viable implants of sarcoma 180
From 5 000 to 60 000 r/air (60 000 r equal to lethal dose for tumor fragments grown in a culture medium <i>in vitro</i>)	Implants produced neither tumor nor immunity <i>i.e.</i> the immunizing properties of the tumor grafts were destroyed

It was thus demonstrated that, in order to induce a resistant state in the experimental animal, *i.e.*, immunity to subsequent viable tumor grafts, the tumor implants had to be attenuated, but not destroyed, by a relatively specific dose of radiation

The question arose whether or not this conclusion applies as well to tumors of known genetic origin grown in inbred strains of animals. Such a condition would correspond to the use of spontaneous tumors. Accordingly, in further experiments, an inbred strain of rats and a tumor which originated in the same strain were used. The results obtained are summarized as follows

SUMMARY OF RESULTS WITH A RETICULUM CELL LYMPHOSARCOMA AUTOGENOUS TO THE STRAIN

<i>Dosage Applied to Implants in vitro</i>	<i>Effects of Irradiation</i>
Up to 2000 r/air	Implants produced tumors
From 2 200 to 2,600 r/air	Implants produced no tumors but rendered about 65 per cent of the animals immune to subsequent viable implants
From 2 800 r/air up	Implants produced neither tumor nor resistance, <i>i.e.</i> , the immunizing properties of the tumor grafts were destroyed

Further experiments are planned to investigate a variety of tumors grown in inbred strains of animals as to their immunizing ability after attenuation with specific doses of radiation. Such a study may serve as a basis of classification of tumors into those with and without ability to induce a state of resistance to malignant growth

The present report has to do with the determination of the radiosensitivity of the same type of tumor originating spontaneously in two different inbred strains of animals

METHOD AND MATERIAL

Two inbred strains of mice, dba and C3H, and tumors originating in these strains were used in these experiments. Mice of the dba strain were obtained from the Roscoe B Jackson Laboratory, Bar Harbor, Maine. This strain has been inbred since 1918. In 1920, a tumor arose

¹ From the Cancer Research Laboratory, Department of Hospitals and Laboratory of Cellular Physiology, New York University, New York.

Presented at the Thirty-second Annual Meeting of the Radiological Society of North America, Chicago, Ill., Dec 1-6 1946. These experiments were aided by grants obtained from the Ella Sachs Plotz Foundation for Scientific Investigations and from Mr J C Brownstone

TABLE I TUMORS PRODUCED BY NON-IRRADIATED CONTROL IMPLANTS IN dba STRAIN OF MICE

Experiment Number	Latent Period (days)	Average Initial Tumor Size (mm)	Period of Tumor Growth (days)	Average Size of Tumors (mm)	Remarks
1	8	4 × 3 × 2	12	24 × 19 × 10	Each experiment included 8 to 10 mice. Therefore the sizes recorded in this table represent averages of 8 or 10 tumors. The tumors were measured in three dimensions. The mice were killed when the tumors started to break through the skin.
2	6	5 × 4 × 2	14	27 × 21 × 12	
3	7	6 × 4 × 3	13	28 × 19 × 12	
4	5	3 × 2 × 2	14	31 × 16 × 16	
5	6	4 × 3 × 3	12	28 × 15 × 10	
6	6	4 × 3 × 2	13	30 × 15 × 12	
7	7	5 × 3 × 3	12	27 × 17 × 12	
8	8	6 × 4 × 3	15	30 × 15 × 10	
9	6	4 × 3 × 2	12	28 × 14 × 12	
10	6	5 × 3 × 2	16	30 × 22 × 14	
11	5	4 × 3 × 3	14	28 × 19 × 11	
12	7	6 × 4 × 3	13	27 × 15 × 12	
13	6	5 × 4 × 2	14	29 × 16 × 14	
14	6	4 × 3 × 3	12	28 × 15 × 12	
15	5	3 × 3 × 2	14	27 × 22 × 11	

spontaneously in a dba mouse and upon microscopic examination was diagnosed as adenocarcinoma. It has been carried on since its discovery by means of successive transplants. In mice of the strain in which it originated it gives 100 per cent "takes." It grows rapidly, producing a tumor about 10 mm in diameter four to five days following inoculation of the graft. The tumor kills the animal within two to three weeks, by which time it measures 30 to 40 mm in diameter. It becomes hemorrhagic within ten to twelve days. It is soft in consistency.

The C3H strain of mice was established by Dr. Leonell C. Strong² of Yale University in 1920 and has been inbred since. This strain of mice has proved to be highly susceptible to spontaneous tumors of the mammary gland. Such a tumor, histologically diagnosed as an adenocarcinoma, was used for the present experiment, by transplanting from animal to animal of the same strain. The tumor "takes" were 90 to 100 per cent. No spontaneous regression of this tumor has ever been observed. The rate of growth is slower than that of the tumor in the dba strain, the latent period, *i.e.* the time elapsing between the implantation of the graft and the occurrence of a measurable tumor, about 8 mm in diameter, being ten to twelve days.

The tumor grows progressively at a slow rate, measuring 25 to 30 mm in diameter in five to six weeks. It is firm in consistency, encapsulated, and becomes hemorrhagic when it reaches a large size.

The first task was to determine the dose of x-radiation applied *in vitro* which would prevent an implant from producing a tumor in the animal organism. The same technique was used as in previous experiments (1). The surface portion of a eight- to ten-day tumor of the dba strain or of a twelve- to fourteen-day tumor of the C3H strain was cut with sharp scissors into fragments about 15 to 20 mm in diameter and weighing about 10 to 15 mg each. A portion of these tumor fragments was used for implantation into a number of control mice. Others were spread on a number 1 round cover slip attached to a mica sheet, covered with a Maximow slide, sealed with paraffin, and irradiated. The radiation was applied by a pulsating potential oil-cooled Coolidge tube. The radiation factors were 200 kv, 20 ma, 0.5 mm Cu plus 1.0 mm Al filtration, 0.9 mm Cu h.v.l. The distance of the tumor fragments from the target was 12.5 cm, and the average intensity was 604 r in air per minute. In figuring the dose received by the tumor fragments, the absorption of the radiation by the covering glass and mica sheet, which was about 10 per cent, was taken into consideration. The dose of radiation in each case was applied in a single exposure. Within fifteen

² I take this opportunity to express my sincere thanks to Dr. Strong for his kind co-operation in supplying mice for this study.

Further Studies on the Relation Between Radiation Effects, Cell Viability, and Induced Resistance to Malignant Growth

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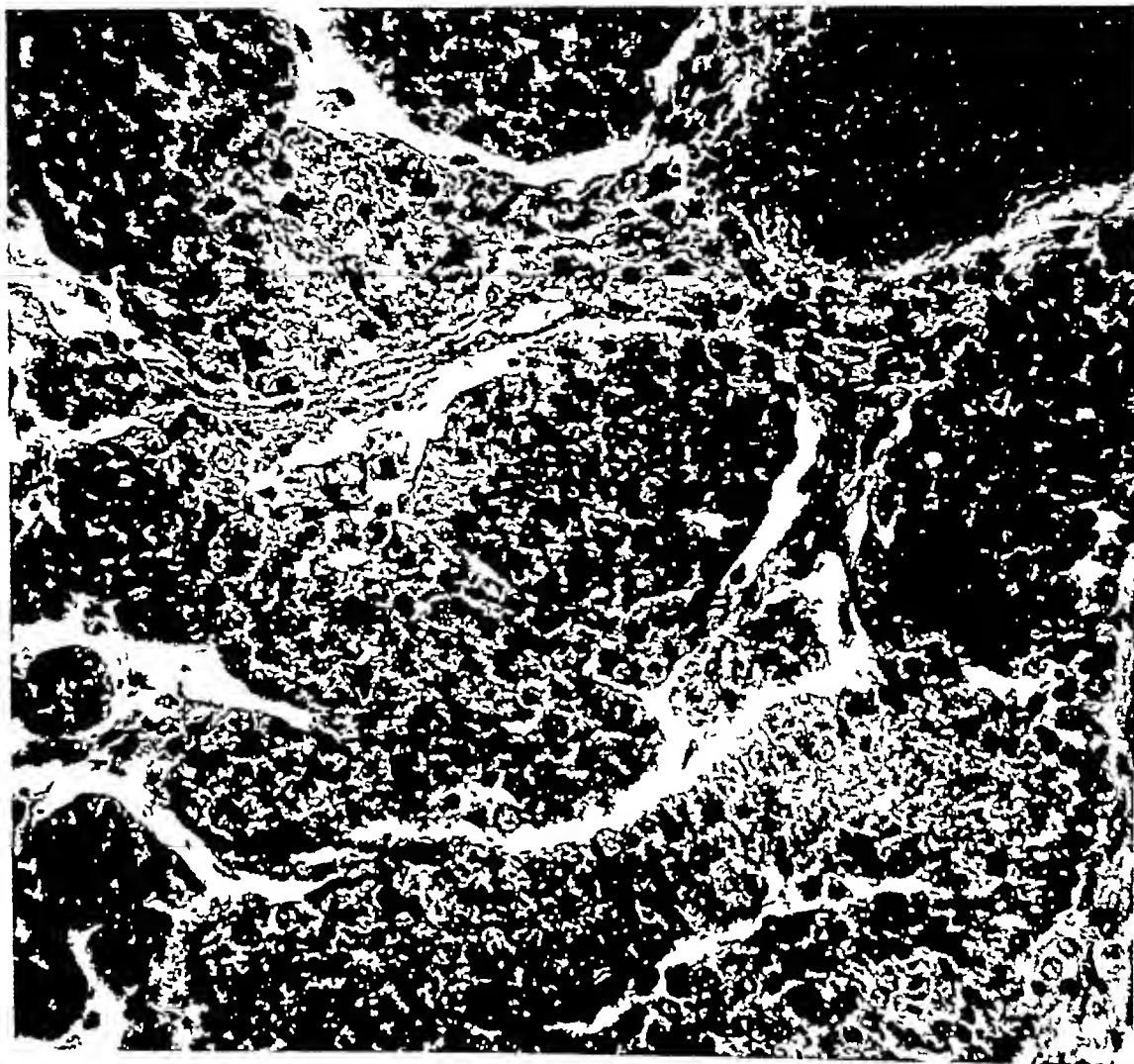


Fig 1 Mammary adenocarcinoma grown in the dba strain of mice $\times 425$

observation deserves special consideration in regard to the problem of recovery following irradiation. For example, it is apparent that an implant exposed to 4,500 r in air was able to produce a tumor of a large size following a latent period as long as fifty four days. The question thus arises whether, after that interval, the irradiated tumor cells recovered following this massive dose to such an extent as to be able to propagate and produce a tumor, or whether a few cells escaped injury and, in order to produce a tumor of a detectable size, required a longer time. Further reference to this question will be made later.

TUMOR GROWTH IN C3H MICE

Table III sets forth the characteristics of the tumor growth in mice of the C3H strain following the inoculation of non-irradiated implants. The latent period varied between ten and twelve days. Within this period the implants produced tumors ranging between 2 and 3 mm in diameter. Within thirty to forty days, the average tumor size was between 35 and 40 mm (diameter).

In Table IV are recorded the characteristics of the tumor growth produced by irradiated implants in the C3H animals. Irradiation of the tumor grafts with doses

TABLE II TUMORS PRODUCED BY IRRADIATED IMPLANTS IN dba STRAIN OF MICE
(200 kv, 20 ma, 0.5 mm Cu + 1 mm Al filter, hv 1.09 mm Cu)

Experiment Number	Dose (r in air)	Latent Period (days)	"Takes" (per cent)	Average Initial Tumor Size (mm)	Period of Tumor Growth (days)	Average Size of Tumor (mm)
1	500	6	100	3 × 3 × 2	12	28 × 18 × 14
2	1 000	6-8	100	3 × 3 × 2	12	25 × 18 × 12
3	1,500	9-12	100	3 × 2 × 2	14	26 × 13 × 11
4	2,000	12-15	100	4 × 3 × 2	25	26 × 12 × 12
5	2 500	12-15	100	3 × 2 × 2	26	25 × 14 × 10
6	3,000	19-24	77.5	3 × 3 × 2	35	26 × 15 × 11
7	3,500	22-41	55.5	4 × 3 × 2	61	24 × 16 × 12
8	3 700	24-41	55.0	3 × 3 × 3	64	25 × 14 × 11
9	4 000	26-46	50.5	4 × 3 × 2	66	24 × 14 × 10
10	4,200	29-48	33.3	3 × 3 × 2	68	25 × 12 × 9
11	4 500	54	11.1	4 × 3 × 3	73	21 × 16 × 12
12	5 000	0	0	0	0	0

REMARKS Each experiment included 12 to 15 mice. The sizes recorded represent averages of 12 to 15 tumors. The mice were killed when the tumors started to break through the skin.

to twenty minutes after irradiation, the tumor fragments were implanted into animals midway between the groin and the axilla by means of a trocar. Non-irradiated control implants were similarly implanted.

Both male and female mice were used in these experiments, weighing about 20 to 25 gm. The animals were fed with Purina dog chow and water *ad libitum*, with fresh carrots two to three times weekly. As criteria of the radiation effects, the latent period, the number of "takes," and the size of the tumors produced were taken into consideration. The same criteria were applied to tumors produced by non-irradiated implants in the control animal.

Histologically the tumor grown in the dba strain (Fig. 1) is a rather differentiated adenocarcinoma with instances of intra-acinar papilliform growth and variable development of stroma. It shows little tendency to necrosis, but a great tendency to hemorrhage. The nuclear structure is rather uniform, usually with reticular oval nuclei. There is a moderate tendency to hyperchromatism.

The tumor of the C3H strain (Fig. 2) is a solid type of epithelial growth with an alveolar arrangement of strands of tumor cells, scant stroma, polymorphous hyperchromatic nuclei, and a tendency to necrosis.

TUMOR GROWTH IN dba MICE

In Table I are recorded the characteristics of the tumor growth in controls of the dba strain. The latent period is seen to be between five and seven days. The average tumor size within this range is between 3 and 5 mm in diameter. Within twelve to sixteen days the average tumor measured between 25 and 35 mm in diameter. At this stage the tumors started to ulcerate and bleed. The animals were therefore killed and the experiment was terminated.

Doses up to 1,000 r in air applied to the tumor implants did not exert any apparent effect on their growth in the animal body. No increase in the latent period or decrease in the rate of growth of these implants was noticed as compared to non-irradiated control implants. As is shown in Table II, the first manifestation of radiation effect was observed in the latent period. Starting with a dose of 1,000 r in air, the latent period was prolonged with increase of the amount of radiation applied to the tumor graft, increasing from the usual six-day period to fifty-four days within the dose range of 1,000 to 4,500 r.

The average tumor size (initial and at the end of the experiment) produced by the irradiated implants showed no significant difference as compared to tumors produced by non-irradiated control implants. This

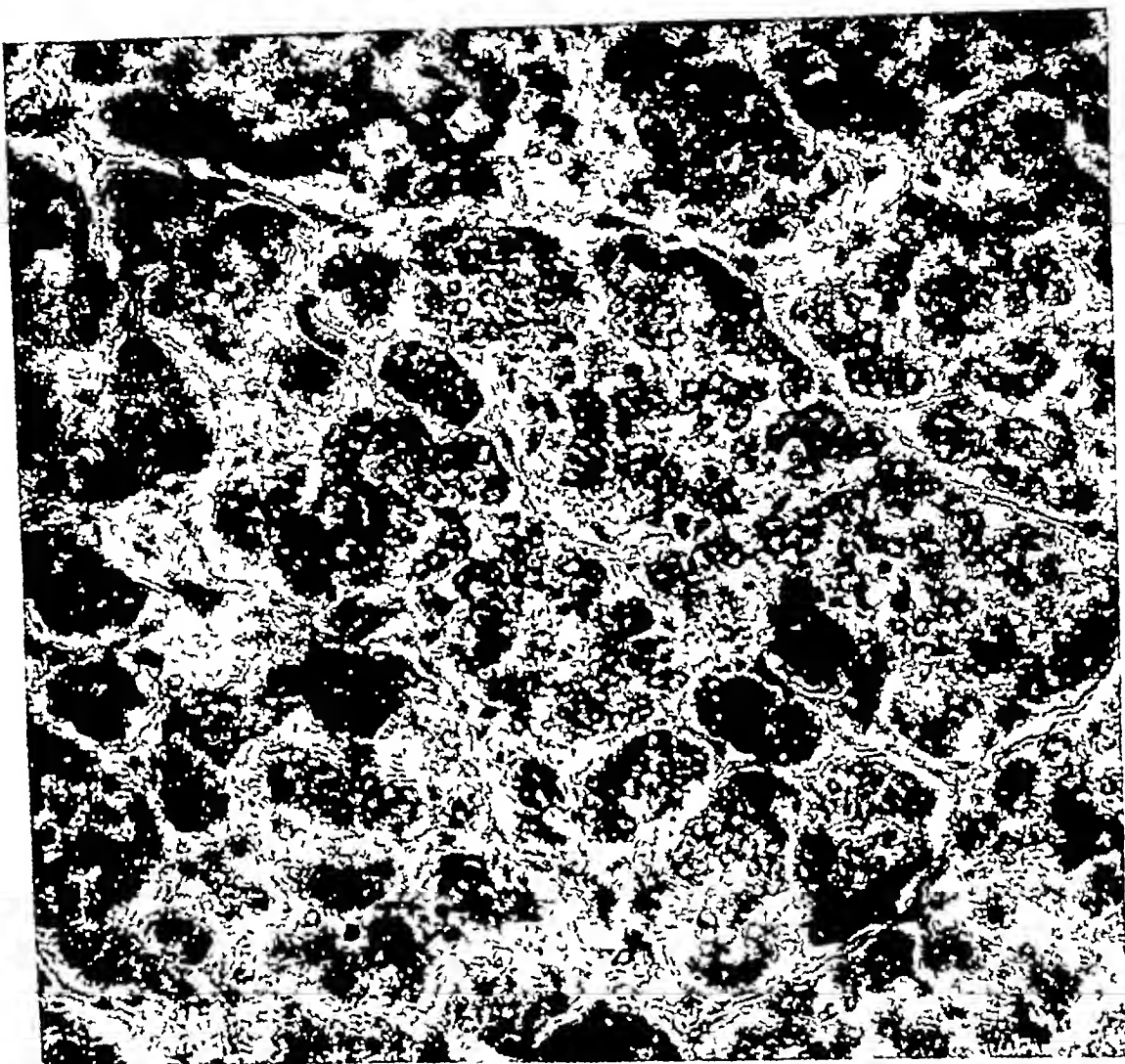


Fig 2 Mammary adenocarcinoma grown in the C3H strain of mice $\times 425$

days, with death of the animals shortly afterward. The latent period for implants of the adenocarcinoma grown in the C3H strain of mice is almost twice as long, namely ten to twelve days, and a longer time is therefore required to produce a tumor which will kill the host. Thus the average period of tumor growth in the C3H strain before death of the animal is about thirty to forty days as compared to twelve to sixteen days in the dba strain.

For the adenocarcinoma grown in the dba mice, a dose of 5,000 r in air was required to prevent the implant from producing a tumor, while for the adenocarcinoma grown in the C3H strain a dose of 2,700 r

in air was sufficient to produce the same result.

Two points of major interest for radiation effects, particularly in therapy, emerge from the observations made in these experiments: (a) the radiosensitivity of tumors of similar histological structure, (b) the recovery process of tumor cells partially affected by radiation.

The radiosensitivity of a tumor is determined by the relationship between a given quantity of radiant energy and the biological effect which it produces. The accurate measurement of radiation presents no problem, so that it devolves upon the precise indication of the biological response

TABLE III TUMORS PRODUCED BY NON-IRRADIATED CONTROL IMPLANTS IN C3H STRAIN OF MICE

Experiment Number	Latent Period (days)	Initial Tumor Size (mm)	Period of Tumor Growth (days)	Average Size of Tumors (mm)	Remarks
1	10	2 × 2 × 2	28	29 × 11 × 6	Each experiment included 12 to 15 mice. The tumor sizes reported in this table represent the average of 12 to 15 tumors
2	11	3 × 3 × 2	38	32 × 14 × 8	
3	10	3 × 2 × 2	45	39 × 18 × 12	
4	12	4 × 3 × 2	39	31 × 15 × 10	
5	12	3 × 3 × 3	42	35 × 20 × 14	
6	9	2 × 2 × 2	37	18 × 18 × 15 (I) 12 × 6 × 6 (II)	
7	12	4 × 3 × 3	43	38 × 19 × 11	The mice were killed when the tumors started to break through the skin
8	12	4 × 3 × 2	51	39 × 25 × 14	
9	10	3 × 2 × 2	43	37 × 18 × 10	
10	12	3 × 3 × 2	41	38 × 17 × 12	
11	12	3 × 3 × 3	38	37 × 15 × 10	
12	11	3 × 3 × 2	42	39 × 18 × 12	
13	10	3 × 3 × 2	39	40 × 18 × 15	
14	12	4 × 3 × 2	43	41 × 17 × 14	
15	12	3 × 3 × 3	37	38 × 18 × 16	

TABLE IV TUMORS PRODUCED BY IRRADIATED IMPLANTS IN C3H STRAIN OF MICE
(200 kv, 20 ma 0.5 mm Cu + 1 mm Al filter, h v l 0.9 mm Cu)

Experiment Number	Dose (r in air)	Latent Period (days)	"Takes" (per cent)	Average Initial Tumor Size (mm)	Period of Tumor Growth (days)	Average Size of Tumors (mm)
1	500	11	100	3 × 2 × 2	35	31 × 24 × 14
2	1,000	12-15	100	4 × 2 × 2	38	30 × 24 × 12
3	1,500	14-28	85	3 × 3 × 2	43	27 × 15 × 10
4	1,800	14-32	50	4 × 3 × 2	48	26 × 14 × 9
5	2,000	16-34	50	3 × 3 × 3	62	24 × 14 × 8
6	2,300	21-38	50	4 × 2 × 2	66	22 × 12 × 9
7	2,500	29-43	37.5	4 × 3 × 2	69	21 × 14 × 9
8	2,600	33	10	3 × 3 × 2	68	27 × 12 × 8
9	2,700	0	0	0	0	0

REMARKS Each experiment included 12 to 15 mice. The sizes recorded represent averages of 12 to 15 tumors. The mice were killed when the tumors started to break through the skin.

up to 1,000 r did not exert any appreciable effect, either on the latent period or on the average tumor size. As in the experiments on the dba strain, the first effects were apparent with a dose of 1,000 r. This was again manifested by an increase of the latent period from the usual ten to twelve days up to fifteen days, progressing with the increase of the x-ray dose to thirty-eight days for implants irradiated with 2,600 r in air.

As to the average tumor size at the end of the experiment, there was no appreciable difference between tumors produced by irradiated implants and non-irradiated control implants. This observation, noted also in the experiments with the dba strain of mice, raised the same question of recovery following irradiation.

DISCUSSION OF RESULTS

A comparison of the observations made from these experiments with two inbred strains of mice and tumors autogenous to these strains reveals the following.

The tumors, although both histologically diagnosed as mammary adenocarcinoma, differ markedly as regards their growth potency and their radiosensitivity. These findings are apparent on a comparison of the latent periods and of the threshold doses of x-radiation, as shown in Tables II and IV and illustrated in graph form in Figure 3.

The implants of the mammary adenocarcinoma grown in the dba strain of mice have a latent period of five to six days and produce tumors averaging from 30 to 35 mm in diameter within twelve to fifteen

As suggested above, this phenomenon is of importance for radiation therapy. In some cases and not in others, the dormant cells attenuated by certain doses of radiation may regain their growth potentiality and ultimately produce a tumor of a size comparable to that produced by non-irradiated cells. In this connection, reference may be made to the observation that viable cancer cells were present in human breast cancers which had been treated with high doses of radiation as much as one year previously (5). This observation has a direct bearing on the results presented in this paper.

CONCLUSION

In conclusion it may be stated that a more precise evaluation of the criteria for the radiosensitivity of a given type of tumor is indicated. It appears that histologic classification alone is an inconclusive guide to the specification of the proper therapeutic dose for any given tumor. In determining the threshold dose of radiation, due consideration should be given to biological factors characteristic of the tumor. Further studies along these lines are in progress. The phase of this work bearing on the production of immunity by means of attenuated implants is in progress and will be reported in a subsequent paper.

NOTE The doses of roentgen rays determining the radiosensitivity of the tumors used in this investigation are obtainable under the experimental conditions outlined in the text. No references are available in the literature to these tumors under the conditions of the experiments here recorded.

The author wishes to express deep appreciation to Carl B. Braestrup, Senior Physicist, Department of Hospitals, and his associates for their cooperation in supplying the physical factors, to Dr. Ira I. Kaplan, Director of the Radiation Therapy Department, Bellevue Hospital, for the use of the x-ray apparatus, to C. Serber and B. Carl for administering the radiation treatments, and to Miss Annabelle Goldberg for laboratory assistance.

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444 East 52nd St.
New York 22, N. Y.

DISCUSSION

Friedrich Ellinger, M.D. (Brooklyn, N. Y.)
Dr. Goldfeder's paper offers much material for discussion, presenting, as it does, evidence of immunity, recovery, and radiosensitivity. I am going to restrict my comments to the problem of radiosensitivity.

I believe that these observations present an interesting step forward in the understanding of an all important problem. It is generally recognized that the particular radiosensitivity of malignant tumors means success or failure in radiation therapy. The analysis of the radiosensitivity of tumors has brought to light a number of factors, of which the degree of differentiation of the malignant tissue and the importance of the tissue of origin have been recognized as predominant.

In the light of present-day knowledge, tumors arising from radiosensitive tissues are considered as more radiosensitive than those originating from radioresistant tissues. The former are classified as constitutionally radiosensitive tumors, while the latter are considered as constitutionally radioresistant. This grouping of malignant tumors into constitutionally radiosensitive and constitutionally radioresistant permits a gross appraisal of their response to irradiation. The degree of differentiation, furthermore, determines to a large extent their individual radiosensitivity within these groups.

However, it is clinically well known that, in spite of identical morphologic and topologic appearance of tumors, considerable differences in their response to irradiation may occur, for which no explanation is available so far. Dr. Goldfeder's observations seem to offer an answer to this problem by demonstrating the importance of the genetic make up of the tumor host for the response of morphologically and topologically identical tumors in mice. I would like to emphasize that her procedure of exposing the implant *in vitro* and

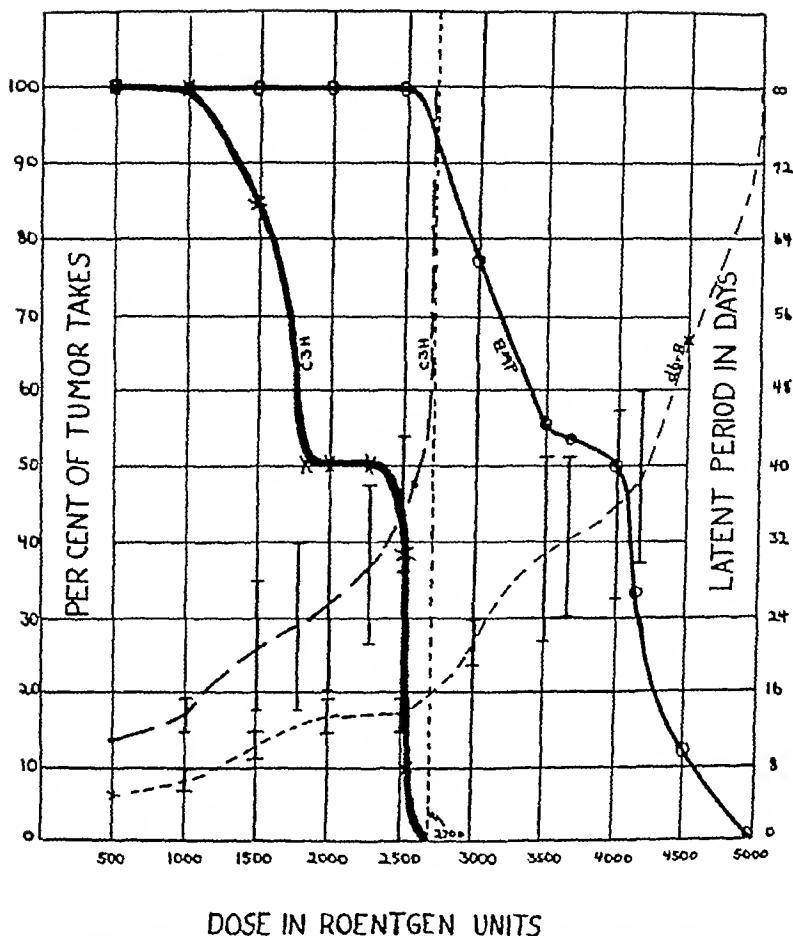


Fig 3 Graph showing the latent periods and percentages of takes of implants of mammary adenocarcinomas grown in dba and C3H strains of mice following a single exposure to roentgen rays. The solid lines represent the percentage of 'takes,' the dotted lines the latent periods.

to determine with exactness the radiosensitivity of a given type of tumor. The customary biological indication is the destruction of viable tissue cells either *in vitro* or *in vivo*, so that the radiosensitivity has been measured in terms of the threshold or lethal doses. Thus, one might expect to obtain sensitivities of the same order for tumors of the same type as manifested by threshold doses of the same order of magnitude. In the experiments presented here, however, the threshold doses for two analogous mammary adenocarcinomas grown in their respective inbred strains showed a considerable difference in their radiosensitivity. How are we to account for the difference in radiosensitivity of these two tumors, both diag-

nosed as adenocarcinomas and each being autogenous to the strain in which it was grown? Are the biological factors which determine radiosensitivity characteristic of the tumor or of the host? In the light of these experiments, one may venture to state that certain intrinsic factors exist controlling the potentiality of tumor growth independent of histologic structure.

In reference to the recovery processes, it is of interest to note that tumor fragments of the dba strain, exposed to such high doses as 4,500 r in air, were able to produce tumors after as long a latent period as fifty-four days, while tumor fragments of the C3H strain of mice exposed to 2,600 r in air were able to do so after thirty-eight days.

Cerebral Angiography

For a good many years, dating well back in the past quarter century, various segments of the circulatory system have been subjected to x-ray examination following the introduction of opaque material into the blood stream. At the outset this form of examination was limited to the preparation of arteriograms and phlebograms of extremity vessels in the case of peripheral vascular diseases. Bolder attempts to use halogenated oil in small quantities to observe the nature of blood currents within the beating heart were sufficiently well advanced to be presented at the International Congress of Radiology held in Chicago in 1937, and there have been several exhibits at roentgenological meetings to demonstrate the diagnostic possibilities which attend the introduction of opaque material into the abdominal aorta and its branches by means of direct arterial puncture. More elaborate perfusion techniques designed to permit investigation of the circulation through the chambers and great vessels of the heart itself have come into fairly wide vogue. This has been accomplished by means of rapid injections of concentrated halogenated substances into large peripheral veins and also by introduction of the material close to the right auricle by way of sizable catheters slipped down through the veins which empty into that structure.

The great rapidity of circulation time, the speed with which opaque materials are diluted by the blood stream, and the necessity for great caution in avoiding thrombosis and the extravasation of the opaque medium have served to prevent all of these highly specialized techniques from being applied very widely in comparison to the enormous volume of diagnostic radiological

procedures which are conducted throughout the world each year.

Egas Moniz is to be credited with the first published attempts to examine the cerebral circulation in living man by means of opaque perfusion. His original report appeared in July 1927 (*L'encéphalographie artérielle, son importance dans la localisation des tumeurs cérébrales*. *Rev. neurol.* 2: 72-90, 1927). Following that beginning, made just twenty years ago, cerebral angiography has grown in favor as a useful device in intracranial diagnosis at a rate which is appropriately related both to the inherent hazards of the procedure and to the brilliant diagnostic results which it is capable of producing.

Although perfusion of the cerebral vessels with an opaque substance can be performed with little or no risk to the patient, and will provide skull roentgenograms of great diagnostic value, it does not follow that this method of study should ever be used as extensively as many other accepted methods of examination. For reliable end-results, a superlative degree of co-operation between the radiologist and his neurosurgical colleague is essential. The procedure is one which should be used only when simpler methods of examination have failed to answer with sufficient accuracy some difficult problem of intracranial diagnosis. Its utility is very largely limited to investigation of the circulation within the supratentorial portion of the cranial cavity. While it is possible to inject the major vessels in the posterior fossa of the skull, the technic involved is considerably more difficult except in those rare instances when introduction of the opaque material by the usual internal carotid route results in adequate filling of

re-implanting it into a new host of the same strain excludes all possible influences of the tumor bed

The demonstration of the importance of the genetic factor in the radiosensitivity of malignant tumors, accounting for as much as 50 per cent difference, appears equally significant from the theoretical and the clinical standpoint. The observations of Dr Goldfeder offer a new and strong argument in favor of individualization and against schematization in radiation therapy of malignant tumors

Paul C Aebersold, Ph D (Oak Ridge, Tenn)

This type of experimentation is necessary in understanding the problems of growth. I would like to add that it ties in with what Dr Kamen had to say yesterday, that there is a biochemical factor produced by radiation. This was demonstrated in Dr Goldfeder's experiments, although we don't understand what has happened, by the fact that putting an irradiated transplant into an animal causes some degree of immunity to a subsequent transplant. It follows that some biochemical factor is liberated by an irradiated cell which can then affect the growth of other cells.

The important point is to get more information of this type and then to seek to determine, as Dr Kamen and others are doing, what is the biochemical growth-blocking factor produced by irradiating a cell. That is, there is some enzyme or other biochemical factor necessary for normal

growth which is blocked in its action as the result of the irradiation.

Dr Goldfeder's work aims at observing how the biochemical agent liberated by a group of cells affects the growth of another group of cells introduced into the same host. By isotopic tracer or biochemical methods we should investigate this type of factor more thoroughly.

Anna Goldfeder, Sc.D (closing) I wish to thank Dr Aebersold. He has brought out the point of immunity to malignant growth. When I started my experiments, my idea was not to utilize this procedure to immunize animals against malignant growth but, as I have mentioned, to compare the effects of radiation *in vitro* and *in situ*. When I looked for an explanation why a very large dose is necessary to destroy tissue cells *in vitro* when a much smaller dose will prevent their proliferation *in situ*, I utilized the phenomenon that if a tumor implant fails to produce a tumor, or if a tumor regresses spontaneously, the host becomes immune or resistant to further viable tumor grafts. Such a phenomenon was, in fact, produced by tumor grafts attenuated with specific doses of radiation. The factor which produces the resistant state—whether it is of a chemical nature or is a virus or of any other specificity—is not as yet determined. The isolation of such a principle from a tissue cell—one which could produce immunity to malignant growth—would be a discovery of the first importance.

SUMARIO

Efectos de los Rayos X sobre los Tumores Mamarios Autógenos en Razas Entrecruzadas de Ratones

Los experimentos ejecutados en ratones de dos razas entrecruzadas, dba y C3H, se proponían determinar el efecto de los rayos X aplicados a implantes de tumores antes de inocularlos.

Los tumores provocados en las dos razas eran, histológicamente, semejantes, siendo en ambas adenocarcinomas mamarios, pero variaron con respecto al período de latencia consecutivo al implante y en la velocidad de su desarrollo. También discreparon en su radiosensibilidad. Para el tumor de desarrollo más rápido (en la raza dba) se necesitó una dosis de 5,000 r (en el aire) para impedir que el implante produjera un tumor en tanto que en el otro bastó con una dosis de 2,700 r para pro-

ducir el mismo efecto. A juzgar por esto, existen ciertos factores intrínsecos que rigen la potencialidad de la carcinogenia aparte de la estructura histológica.

Se observó igualmente que los implantes neoplásicos expuestos a altas dosis de rayos X eran capaces de producir tumores tras un período excesivamente largo de latencia (54 días, comparado con un período normal de 5 a 7 días en una raza y 38 días, comparado con un período normal de 10 a 12 días en la otra), lo cual sugiere que en algunos casos las células atenuadas por la radiación pueden recuperar su potencialidad de desarrollo y producir por fin un tumor comparable al producido por las células no irradiadas.

PITTSBURGH ROENTGEN SOCIETY

The newly elected officers of the Pittsburgh Roentgen Society are Dr H N Mayhew of Pittsburgh, President, Dr Joseph Danzer of Oil City, Vice-President, Dr R P Meader of Pittsburgh, Secretary-Treasurer

UROLOGY AWARD

The American Urological Association offers its annual award of \$1,000 (first prize \$500, second prize \$300, and third prize \$200) for essays on the result of some clinical or laboratory research in urology. The competition is limited to urologists who have been in such specific practice for not more than five years and to residents in urology in recognized hospitals. Full particulars may be obtained from the Secretary, Dr Thomas D Moore, 899 Madison Ave, Memphis, Tenn. Essays must be in his hands before March 1, 1948.

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A communication from the American Friends Service Committee tells of the need of scientific and technical books to reconstruct the library of the Technical Institute at Helsinki, Finland, destroyed by bombing during the war. In the remarkable efforts for recovery that the Finns are making, the lack of technical library facilities is a serious handicap. It would be a practical act of friendship to a nation that holds America in high regard if Americans should contribute good technical books and periodicals to this library.

Any such gifts should be marked for the Institute of Technology, Helsinki, and sent to the Legation of Finland, 2144 Wyoming Ave, N W, Washington, D C. Dr K T Jutila, the Finnish Minister, will arrange for their shipment to Finland.

Book Reviews

PRACTICAL X-RAY TREATMENT By ARTHUR W ERSKINE, M D. A volume of 155 pages with 22 illustrations. Published by The Bruce Publishing Company, St Paul and Minneapolis, 3d edition 1947.

Though the author does not attempt to answer the several questions raised in the introduction to the Second Edition of his *Practical X-ray Treatment*,

he has succeeded in enhancing the concentrated information found in the earlier editions of the work. The book is a practical guide for the student or roentgenologist seeking useful material on roentgen therapy presented in a concise, clear, but admittedly somewhat dogmatic manner. It enables the experienced radiologist to compare his own results with those obtained by the author's methods.

The first eight chapters deal primarily with the physical side of roentgenology, covering current apparatus, protection, measuring instruments, both direct and indirect, factors affecting skin dosage and depth dosage, standard techniques, scattering and distribution, determination of skin dose, and the effects of radiation on normal and abnormal tissues. Three techniques at 135 kv p and one at 200 kv p are described, with various modifications. Included are fourteen useful depth-dose charts covering various field sizes and anode skin distances through a range of qualities from half-value layers of 1.0 mm aluminum to 2.0 mm copper.

There follow chapters on the treatment of skin diseases, infections, non-malignant, and finally malignant neoplasms. A philosophical chapter entitled "The Cancer Problem and the Radiologist" is an erudite discussion by one who has dealt with cancer patients from the early days of radiation therapy.

One criticism of the work might be its brevity in the actual description of the treatment of malignant disease. There is still much room for extension in that detail without defeating the avowed purpose of the book.

In Memoriam

EDWARD EVERETT ROWELL, M D

1878-1947

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subtentorial vessels by way of the posterior communicating artery

It is felt by some workers in this field that the procedure may be simplified considerably if indirect puncture of the carotid is accomplished through the intact skin, thus obviating the necessity for surgical exposure of the vessel. There are those who believe, however, that when the information to be derived from angiography is sufficiently important to the clinical problem in hand, the niceties of technic which are made possible by surgical exposure of the internal carotid, as well as the prevention of possible and undesirable extravascular leakage, amply justify the more elaborate procedure of direct injection into the blood stream. The details of both technics are readily available in recently published articles on the subject.

As yet, no truly ideal material has been made available for this particular type of contrast radiography. Substances which are readily tolerated in peripheral vessels, as well as the circulation through the heart, cannot be used in the cerebral circulation if they are known to produce profound brain irritation. One opaque substance which is singularly free from this undesirable property, thorotrast, is used with justifiable reluctance by radiologists and neurosurgeons because of its inherent and prolonged radioactivity. Thorium dioxide is excreted very slowly indeed after injection, the major portion being stored in the reticulo-endothelial system. Once more, if the procedure is begun with careful consideration for the necessity of the examination and the likelihood that it will produce information of great value, careful planning of the technic to be used will permit the satisfactory employment of a sufficiently small amount of thorium dioxide to prevent the accumulation of amounts within the body which can possibly constitute a threat of serious toxic end-results. If used in amounts which have been shown to be innocuous, thorium dioxide (thorotrast) is a suitable contrast material.

Cerebral angiography owes its diagnostic successes to three characteristic groups of

findings, each of which has peculiar advantages. In the case of intracranial lesions which involve the circulatory system primarily, it is possible by means of the angiographic procedure to obtain direct information regarding the location and character of the lesion. For example, cerebral aneurysms, whether they involve the internal carotid in its cavernous sinus segment at the base of the brain, or more peripheral branches, can be observed with the greatest ease and clarity in contrast to the less definitive signs which depend upon erosion of neighboring bone. By the same token, obliteration of vascular channels, either partial or complete, can be identified and localized with a high degree of certainty. Tumors generously supplied with blood vessels can be seen in their own right in properly prepared roentgenograms when these mazes of tumor vessels are momentarily filled with opaque material. It is possible on the basis of the critical study of resulting roentgenograms to identify the particular tumor involved when cerebral angiograms are available. This is particularly true in the case of most glioblastomas. Over and above the diagnostic findings which are uniquely characteristic of cerebral angiograms, evidences of vascular displacement, comparable to the signs of ventricular displacement obtained in ventriculography, can be utilized advantageously in the localization of intracranial tumors.

The combined neurosurgical and radiological procedure of cerebral angiography has won for itself during the past twenty years a well established position. While it is not a procedure to be used indiscriminately and inadvisedly, there will always be found, in every clinic where any considerable volume of intracranial disease is being apprehended and treated, problem cases which do not lend themselves to less elaborate methods of study. Reserved for use in this field, cerebral angiography represents a significant milestone in the never ending advancement of diagnostic roentgenology.

FRED J. HODGES, M.D.

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RADIOLOGICAL SOCIETIES SECRETARIES AND MEETING DATES

Editor's Note Secretaries of state and local radiological societies are requested to co-operate in keeping this section up-to-date by notifying the editor promptly of changes in officers and meeting dates Address Howard P. Doub, M.D. The Henry Ford Hospital, Detroit 2, Mich

UNITED STATES

RADIOLOGICAL SOCIETY OF NORTH AMERICA *Secretary-Treasurer*, Donald S. Childs, M.D., 607 Medical Arts Bldg., Syracuse 2, N.Y.

AMERICAN RADIUM SOCIETY *Secretary*, Hugh F. Hare, M.D., 605 Commonwealth Ave., Boston 15, Mass.

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AMERICAN COLLEGE OF RADIOLOGY *Secretary*, Mac F. Cabal, 20 N. Wacker Dr., Chicago 6, Ill.

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ALABAMA RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Courtney S. Stickley, M.D., Bell Bldg. Montgomery. Next meeting at the time and place of the Alabama State Medical Association meeting

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ARKANSAS RADIOLOGICAL SOCIETY *Secretary*, Fred Hames, M.D., Pine Bluff. Meets every three months and annually at meeting of State Medical Society

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CHICAGO ROENTGEN SOCIETY *Secretary*, T.J. Wachowski, M.D., 310 Ellis Ave., Wheaton. Meets at the Palmer House second Thursday of October, November, January, February, March, and April, at 8:00 P.M.

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INDIANA ROENTGEN SOCIETY *Secretary-Treasurer*, J.A. Campbell, M.D., Indiana University Hospitals, Indianapolis 7. Annual meeting in May

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IOWA X-RAY CLUB *Secretary*, Arthur W. Erskine, M.D., 326 Higley Building, Cedar Rapids. Meets during annual session of State Medical Society

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ORLEANS PARISH RADIOLOGICAL SOCIETY *Secretary*, Joseph V Schlosser, M D, Charity Hospital of Louisiana, New Orleans 13 Meets first Tuesday of each month

SHREVEPORT RADIOLOGICAL CLUB *Secretary*, Oscar O Jones, M D, 2622 Greenwood Road Meets monthly September to May, third Wednesday 7 30 P M

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BALTIMORE CITY MEDICAL SOCIETY, RADIOLOGICAL SECTION *Secretary*, Harry A Miller, 2452 Eutaw Place, Baltimore

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DETROIT X-RAY AND RADIUM SOCIETY *Secretary-Treasurer*, E R Witwer, M D, Harper Hospital, Detroit 1 Meetings first Thursday of each month from October to May, at Wayne County Medical Society club rooms

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Missouri

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ST LOUIS SOCIETY OF RADIOLOGISTS *Secretary* Edwin C Ernst, M D, 100 Beaumont Medical Bldg Meets on fourth Wednesday of each month, October to May

Nebraska

NEBRASKA RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Ralph C Moore, M D Nebraska Methodist Hospital, Omaha 3 Meetings third Wednesday of each month at 6 P M in either Omaha or Lincoln

New England

NEW ENGLAND ROENTGEN RAY SOCIETY *Secretary-Treasurer*, George Levene, M D, Massachusetts Memorial Hospitals Boston, Mass Meets monthly on third Friday at Boston Medical Library

New Hampshire

NEW HAMPSHIRE ROENTGEN SOCIETY *Secretary-Treasurer* Albert C Johnston, M D, Elliot Community Hospital Keene Meetings quarterly in Concord

New Jersey

RADIOLOGICAL SOCIETY OF NEW JERSEY *Secretary*, Raphael Pomerantz, M D, 31 Lincoln Park Newark 2 Meetings at Atlantic City at time of State Medical Society and midwinter in Newark as called

New York

ASSOCIATED RADIOLOGISTS OF NEW YORK, INC *Secretary*, William J Francis, M D, East Rockaway, L I

BROOKLYN ROENTGEN RAY SOCIETY *Secretary-Treasurer*, Abraham H Levy, M D, 1354 Carroll St, Bklyn 13 Meets fourth Tuesday of every month, October to April

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NEW YORK ROENTGEN SOCIETY *Secretary* Win Snow, M D, 941 Park Ave, New York 28

ROCHESTER ROENTGEN-RAY SOCIETY *Secretary*, Murray P George, M D, 260 Crittenden Blvd, Rochester 7 Meets at Strong Memorial Hospital, third Monday, September through May

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RADIOLOGICAL SOCIETY OF NORTH CAROLINA *Secretary-Treasurer*, James E Hemphill, M D, Professional Bldg, Charlotte 2 Meets in May and October

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Ohio

OHIO RADIOLOGICAL SOCIETY *Secretary*, Cartoll Dundon, M D, 1030 Reibold Bldg, Dayton 2 Next meeting at annual meeting of the Ohio State Medical Association, May 1948

CENTRAL OHIO RADIOLOGICAL SOCIETY *Secretary*, Edward T Kirkendall M D, 700 North Park St, Columbus 8

CINCINNATI RADIOLOGICAL SOCIETY *Secretary* Eugene L Saenger, M D, 735 Doctors Bldg, Cincinnati 2 Meets last Monday of the month, September to May

CLEVELAND RADIOLOGICAL SOCIETY *Secretary-Treasurer*, George L Sackett, M D, 10515 Carnegie Ave, Cleveland 6 Meetings at 8 30 P M on fourth Monday, October to April, inclusive

Oklahoma

OKLAHOMA STATE RADIOLOGICAL SOCIETY *Secretary-Treasurer*, Peter M Russo M D, 230 Osler Building Oklahoma City Meetings three times a year

Oregon

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THE HEAD AND NECK

Penicillin in the Treatment of Infections in the Nasal Passages and Sinuses. Richard E Dunn Australian & New Zealand J Surg 16 163-181, January 1947

This paper is an account of the use of penicillin as an adjunct in the treatment of infections of the nose and accessory sinuses. Before treatment was instituted, x ray studies of the sinuses were made, antral puncture was done, and antral washings were obtained. The treatment was undertaken only in those cases in which the presence of penicillin sensitive organisms were found to be present. In patients with sinus symptoms x ray examination was particularly helpful not only in the diagnosis of sinusitis, but also in determining which sinuses were involved. Only by this means could the most effective method of applying penicillin in a given case be ascertained.

Four methods of administration are described (1) local application by (a) displacement of air from the sinuses, (b) nasal drops (c) antral puncture and instillation or (d) continuous irrigations, (2) intramuscular injection, (3) local application combined with oral administration of sulfamerazine, (4) intramuscular and local application combined.

Initial and repeat roentgenograms were employed to determine the most efficacious route for penicillin administration in a given case as well as to follow the clinical response to treatment.

Six cases are described in detail and a summary of 70 cases is presented in table form. While the majority of the patients claimed relief of symptoms and showed roentgen evidence of improvement, the author believes that the response to other conservative measures would have been equally good. LOUIS BERNSTEIN M D

Adamantinoma of the Maxillary Sinus. Report of Two Cases. George S Richardson Ann Otol Rhin & Laryng 55 914-931 December 1946

Two cases of adamantinoma of the maxillary sinuses are reported, one of which presented an atypical and the other a typical microscopic picture. This tumor has been adequately defined as an "epithelial tumor arising from the odontogenic apparatus or from cells with a potentiality for forming tissues of the enamel organ." The commonest sites are the mandible, maxilla, tibia, and hyphosphyl body probably in that order.

The tumor may arise as a solid growth and become cystic, or it may arise as either a solid or cystic type and so remain. A wide age range is noted, but the greatest incidence is in the late third and early fourth decade of life.

Adamantinoma, like other antral tumors, may be suggested by a careful history, eliciting earlier dental trauma or a unilateral nasal obstruction of long standing with mucopurulent or serosanguineous discharge. Symptoms include fetor occasionally frontal head ache, cranial nerve disturbances involving the first, second, third, fourth and fifth nerves and external deformity.

Chont (Am J Roentgenol 50 480, 1943 Abst in Radiology 42 511 1914) considers adamantinoma quite characteristic roentgenologically. The solid adamantinoma he believes has a monocystic appearance on

the x-ray film, interrupted by small niches on the border of the bony defect. This produces a more or less lobulated appearance and a few fine bone trabeculae to differentiate it from odontogenic cysts with their smooth borders. The polycystic type reveals a honeycomb appearance in the early stage. Tooth elements may or may not be contained, but the round cystic compartments are quite characteristic.

The roentgenologic diagnosis of any antral tumor depends upon the familiarity of the roentgenologist with the behavior of the tumor in that location. Certainly all adamantinomas do not necessarily become encapsulated in a bony shell, nor produce large, bulging external deformities.

The roentgenograms in one of the author's cases showed nothing of significance other than bone destruction, while the other presented certain of the characteristics outlined by Chont, namely a monocystic appearance with small niches in a bony trabecula through the midportion of the sinus, while subsequent films revealed a honeycomb appearance with round, cystic compartments.

Adamantinomas are malignant, invasive, and comparatively slow growing. For a favorable prognosis they must be recognized promptly, be radically and thoroughly treated by early and adequate surgery, and watched frequently for recurrence. Irradiation affords little or no benefit in halting progress of the tumor.

STEPHEN N TAGER, M D

Recurrent Parathyroid Adenoma. A Case Report. Lloyd B Burk Jr Surgery 21 95-101, January 1947

This case report illustrates the recurrence of benign parathyroid adenoma from a transplant of the tumor left in at the first operation.

Diagnosis of hyperparathyroidism in a 31-year-old white male was established through the following roentgenographic changes: (1) prominence of the trabecular pattern and decalcification throughout the entire skeleton, especially the skull, (2) cystic changes in the tibial condyles bilaterally, the lateral condyle of the left femur, the 4th, 5th, 6th and 7th ribs on the right, and the 3d rib on the left, with two fractures, (3) marked calcium deposition in the parenchyma of both kidneys, (4) absence of the lamina dura of the teeth. Laboratory findings confirmed the diagnosis, and a tumor was palpable just to the left of the trachea and above the sternum. At operation, as a safeguard against development of hypoparathyroidism, a small fragment of the adenoma was transplanted beneath the sternothyroid and sternohyoid muscles.

Two years later, the patient was again seen with a tumor at the site of the transplant and recurrent manifestations of hyperparathyroidism. The tumor was excised. Pathologically it resembled the original adenoma, though some of the cells were less typical, showing mild pleomorphic and hyperchromatic changes. Neither tumor is considered malignant. The patient was free of symptoms after the second operation, and x ray examination showed complete recalcification of the skull and partial remineralization of the cervical spine. The cystic areas were nearly recalcified.

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Striking disagreement of the readers with one another regarding the presence or absence of tuberculosis was found. In some cases 20 per cent of the films which were called positive for tuberculosis by one reader were read as negative by another. Furthermore, there was great variation in the ability of an individual reader to be consistent with himself in two independent interpretations of the same set of 14 X 17 inch celluloid films.

Two suggestions are made: (1) that a revision of the method of classifying films is needed, such a revision to be based on an extensive study and actual experimentation, (2) that in mass survey work all films be read independently by at least two interpreters and that all persons whose films are selected as positive or suggestive for tuberculosis by one or the other interpreter be recalled for further study.

L. A. POZNAK, M.D.
(University of Michigan)

Discrepancies Between Clinical-Radiological and Bronchospirometric Findings Raul F. Vaccarezza, Alfredo Lanari and Alberto Soubrié. *Am. Rev. Tuberc.* 55: 128-143, February 1947.

By means of bronchospirometry the functional capacity of each lung can be determined separately. The author presents a series of cases in which the clinical and radiographic findings were at variance with those obtained by bronchospirometry. In each of these the lung appearing more severely involved by disease revealed the better pulmonary respiratory function. Upon analysis, the causes for this discrepancy were found to be as follows:

1. **Pulmonary Factors** Emphysema or diffuse fibrosis may pass unnoticed or be underestimated in the roentgenogram. Small parenchymal lesions may be unobserved.

2. **Bronchial Factors** Bronchial lesions may interfere greatly with ventilation due to partial stenosis.

3. **Pleural Factors** Pleural thickening and adhesions frequently diminish the functional capacity of the corresponding lung. These lesions are not always apparent in roentgenograms.

4. **Changes in the Chest Wall** Muscular atrophy, phrenic paralysis, or pain on one side may seriously affect the pulmonary function.

It is concluded that bronchospirometric examination should be done in all patients who are to be submitted to surgical collapse therapy, since this method may show that the contralateral lung has insufficient functional capacity to allow collapse of the opposite side.

L. W. PAUL, M.D.

Bronchiectasis: A Neglected Disease William M. Kinney. *Dis. of Chest* 13: 33-47, January-February 1947.

The author made the diagnosis of bronchiectasis 59 times with the aid of bronchography during a period of eighteen months while on duty on the general chest service of a naval hospital. During this time 9,754 patients were admitted to the hospital. The incidence of bronchiectasis was thus 0.6 per cent, representing the largest non-tuberculous group of chronic pulmonary diseases. The condition followed pneumonia in 29 cases, upper respiratory infection in 15, asthma in 2, scarlet fever in 2, whooping cough in 2, measles in 1, lung abscess in 1, inhalation of poison gas in 1. In 0

there was no known antecedent illness. The ages by decades for the onset of symptoms were as follows: from 1 to 10 years, 16; 11 to 20 years, 18; 21 to 30 years, 19; 31 to 40 years, 6.

The duration of the symptoms was under six months in 24 cases, 7 to 12 months in 5, 1 to 2 years in 3, 2 to 3 years in 1, 3 to 4 years in 2, 4 to 5 years in 1, 5 to 10 years in 9, 10 to 15 years in 5, 15 to 20 years in 4, 20 to 25 years in 5. The group of 24 with symptoms of less than six months' duration had had a streptococcal pneumonia, contracted during an epidemic at one of the training camps. Cough and expectoration were present in all cases, but in only 2 was the sputum foul. The majority of the patients complained of increased susceptibility to respiratory infections. Hemoptysis and pulmonary hemorrhage were present in 19 cases. Dyspnea on exertion was complained of by 6. Clubbing of the fingers was present in 1 case only.

The roentgen findings in preliminary films are described as thickening and fuzziness of the linear markings in 46, evidences of atelectasis in 28, ring shadows in 12, pneumonic shadows (bronchopneumonia or atypical pneumonia) in 19, and no abnormal shadows in 11.

Bronchograms were necessary for positive diagnoses. For introduction of the iodized oil, the author recommends the supraglottic method for general use as being simple and requiring no special apparatus. The lesions were localized as follows: left lower lobe alone, 23; right lower lobe alone, 13; both lower lobes, 12; right middle lobe alone, 2; both lower lobes and right middle lobe, 2; both lower lobes, right middle lobe, and lingula of left upper lobe, 2; right upper lobe alone, 1; lingula of left upper lobe alone, 1; right middle and right lower lobes, 1; left lower and right middle lobes, 1; both lower lobes and lingula of left upper lobe, 1.

Such complications as acute pneumonitis, pulmonary abscess, empyema, pulmonary fibrosis, and emphysema are inevitable in the long-standing cases and may lead to cor pulmonale. Metastatic abscesses to brain, liver, and bones are not uncommon. Amyloidosis is rare.

The author also discusses prophylaxis and medical and surgical treatment. HENRY K. TAYLOR, M.D.

Residual Mustard Gas Bronchitis: Effects of Prolonged Exposure to Low Concentrations of Mustard Gas Philip Morgenstern, Frank R. Koss, and William W. Alexander. *Ann. Int. Med.* 26: 27-40, January 1947.

Mustard vapor like other irritant gases produces an inflammatory reaction in the mucosa of the respiratory tract. The severity of the inflammatory process will vary with the concentration of the gas, the length of exposure, and the susceptibility of the individual. But although the inflammation is most severe in the upper respiratory tract, decreasing in intensity downward, it is the smaller bronchi and bronchioles which tend to show residual pathologic changes due to the accumulation of secondarily infected secretions and necrotic tissues. The "peribronchial thickening" often noted in the basal portions of the lung fields on roentgenograms may well represent small areas of patchy atelectasis. The stage is then set for the development of bronchiectasis.

Fifty-five out of 85 patients suffering from exposure to mustard gas, on whom lipiodol studies were done, showed definite roentgen evidence of bronchiectasis ranging from slight involvement of a few bronchi in one

THE CHEST

Disseminated Pulmonary Calcification A Report of 113 Cases Robert H High Henry B Zwerling and Michael L Furcolow Pub Health Rep 62 20-29 Jan 3 1947

The literature on pulmonary calcification is reviewed, and a study of 113 cases is presented. In every instance five or more calcareous deposits were present in each lung field scattered over at least half the field. The films were studied by two "readers," and were reviewed by both first separately and then together so that the findings were as objective as possible. Tuberculin and histoplasmin skin tests were made on these patients and interpreted according to well established standards.

Two types of disseminated calcification were recognized: miliary calcification and multiple bilateral calcification. The distinction is interesting, since most observers feel that the miliary type results from hematogenous dissemination of the causative agent, whereas the multiple bilateral type is the result of bronchogenic dissemination. Illustrations of both types are included.

Sixty-four of the 113 cases studied were previously reported by Furcolow, High, and Allen (Pub Health Rep 61 1182 1946) having been found among 6528 school children in Kansas City, Mo. The remaining 49 cases were collected from various sources. The authors analyze each of these groups separately, as well as giving the figures for the two combined. Of the 113 persons showing pulmonary calcifications, 108 were tested with both histoplasmin and tuberculin. 86.1 per cent reacted positively to histoplasmin but not to tuberculin, 10.2 per cent reacted positively to both, 3.7 per cent were negative to both, none gave a positive reaction to tuberculin and a negative reaction to histoplasmin. Summing up these observations, it is found that 96.3 per cent gave positive histoplasmin reactions as compared to 10.2 per cent reacting to tuberculin.

In 69 of the 113 cases or 61.1 per cent the pulmonary calcification was of the multiple bilateral type and in 44 or 38.8 per cent of the miliary type. Calcifications were present in the hilar structures in 73.5 per cent of the former group and in only 50 per cent of the latter. No significant differences were observed in the skin reactions in these two groups.

The authors conclude that their findings constitute strong evidence that disseminated calcifications in the lungs are not frequently caused by tubercle bacilli but probably by the agent producing sensitivity to histoplasmin. Two interesting observations were the lower incidence of chest calcification in Negroes and the demonstration of a definite familial relationship.

An excellent bibliography on pulmonary calcification is appended. To this might be added a paper by Frimann Dahl and Waaler appearing in 1936 as Supplementum 33 Acta radiologica. This was suggested by one of the authors (H. B. Z.).

SYDNEY F. THOMAS, M.D.

Nontuberculous Pulmonary Calcification and Histoplasmin Sensitivity Robert H High Pennsylvania M J 50 384-387 January 1947

Calcareous deposits in the pulmonary parenchyma and tracheobronchial lymph nodes have generally been considered the result of healed tuberculosis. It has been found, however, that many patients with such calcification do not react to tuberculin and that areas of

this country with a high frequency of calcification in the chest are not necessarily those with high mortality rates for tuberculosis.

Earlier investigators were able to demonstrate that pulmonary infections with *Coccidioides immitis* could cause calcification in the chest but no significant correlation could be established between the pulmonary condition and coccidioidin sensitivity. It was noted by Smith (M Clin North America 27 790, 1943) that most cases of histoplasmosis (caused by *H. capsulatum*) had occurred in areas where a high incidence of calcification in the chest was seen and as antigen from this fungus was available, groups of nurses were tested for sensitivity. This was done on the theory that, like coccidioidomycosis, histoplasmosis might occur in an unrecognized benign form which would cause pulmonary calcification. The number of positive reactors to histoplasmin has shown wide variation geographically. It has been found, however, by various observers that far more patients with lung calcification react positively to histoplasmin than to tuberculin. Of one group of 3105 nurses, 294 showed pulmonary calcifications, and of these 63 gave positive reactions to tuberculin, 206 to histoplasmin, 26 to neither. There is as yet, however, no proof that histoplasmin sensitivity is caused by present or past infections with *H. capsulatum*.

It is emphasized that in most instances it is impossible to distinguish between tuberculous and non-tuberculous calcification roentgenographically, though some workers have attempted to show that disseminated or "whetstone-like" calcifications are caused by the agent producing histoplasmin sensitivity.

JOSEPH T. DANZER, M.D.

Tuberculosis Case Finding A Comparison of the Effectiveness of Various Roentgenographic and Photofluorographic Methods Carl C Birkelo, W Edward Chamberlain, Paul S Phelps, Percy E Schools, David Zacks and Jacob Yerushalmy J A M A 133 359-365 Feb 8, 1947

In 1944 the Veterans Administration recognized the need for comprehensive evaluation of different roentgenographic and photofluorographic methods and a Board of Roentgenology, aided by a statistician, was appointed. The Board consisted of two radiologists and three chest specialists. The conditions of mass survey work were simulated as closely as possible for the various techniques employed. Manufacturers provided the machines and made special efforts to produce films of the best possible quality. For each one of 1256 individuals a 14 × 17 inch celluloid film 35-mm and 4 × 10 inch photofluorograms and 14 × 17 inch paper negatives were obtained on the same visit. These sets of films were then interpreted independently by the five members forming the Board of Roentgenology.

An agreement on nomenclature and code for classifying the films into categories as uniform as possible was made before any of the films in the survey were reviewed. Each reader then received only one set of films at a time. The 14 × 17 inch celluloid films were read last in the series and after a wait of two months were again read by each reader.

The results were found to justify the conclusion that no one of the methods, not even the 14 × 17 inch celluloid, is superior for case finding purposes to any other method. The miniature technique showed slight overreading by one reader but it is felt that this handicap can be overcome by personal training.

phragm or stationary grid In the differentiation of extrapleural fluid from effusion in the intrapleural space the following points may be helpful (1) in the erect position, extrapleural fluid does not collect in the costophrenic angle, (2) in the supine position extrapleural fluid does not disperse as a diffuse shadow, but retains the same contour as in the erect position, and (3) a convex lower and anterior border is seen with the larger fluid collections

Six illustrative cases are reported

ELLWOOD W GODFREY, M D

Progressive Scleroderma of the Skin with Cystic Sclerodermal Changes of the Lungs A Dostrovsky Arch Dermat & Syph 55 1-11 January 1947

Progressive scleroderma is a disease that usually affects the skin and underlying musculature Autopsy reports, however, have shown that internal organs, such as the esophagus, lungs, heart, kidneys liver, and endocrine glands may also be affected

The author describes three cases showing that there are characteristic pulmonary changes when the disease affects the lungs Autopsy reports on two of these cases show that the lungs become cystic in their mid portion and basal areas There is an increase in fibrous tissue throughout the lungs and a thickening of the blood vessels There may be adhesions between the lobes to such a degree that they grow firmly together

The radiographic findings in these cases are in no way characteristic of the disease There is an increased amount of fibrous tissue similar to that seen in an old hematogenous infection Some cases may show cystic or cavity-like shadows in the mid and lower portions of the lungs The apices are not usually affected

JOSEPH T DANZER, M D

Human Glanders Report of Six Cases Calderon Howe and Winston R Miller Ann Int Med 26 93-115 January 1947

Six cases of glanders occurring within the space of one year among personnel involved in laboratory research work with *Malleomyces mallei* are reported The diagnosis was substantiated by a significant and sustained rise in the serum titer of agglutinins for *M mallei* in 5 cases and by a less marked rise in titer in the sixth case In 4 cases the complement fixation test also became positive The only other striking laboratory finding was a persistent leukopenia and relative lymphocytosis With recovery the lymphocytosis tended to subside, and the differential count gradually resumed normal proportions

The roentgen findings in 4 cases were similar in that the lesions suggested lung abscess in the early stages, before cavitation and necrosis being fairly well circumscribed and roughly circular in outline In another case the lesion was more suggestive of pneumonitis being somewhat diffuse and infiltrating in character In one case chest films were negative In no instance was there roentgen evidence of pleuritis or pleural effusion

All 6 patients were treated with sulfadiazine because of striking evidence of its efficacy in animals infected experimentally with *M mallei* The indications are that that human infection with *M mallei* is also amenable to sulfadiazine though no definite conclusions can be drawn from so small a series

STEPHEN N TAGER M D

Surgical Treatment of Myasthenia Gravis O Theron Clagett and L M Eaton J Thoracic Surg 16 62-78, February 1947

This article presents a complete discussion of myasthenia gravis, primarily from the surgical point of view The authors have studied 191 cases of the disease of which 32 were treated operatively and followed for at least six months thereafter In 15 cases tumors of the thymus were found In 17 cases, no tumor was found but in 16 of these the gland was enlarged

Before the present study was undertaken, in 1941, no case of a thymic tumor had been unequivocally demonstrated roentgenographically even though all patients had had stereoscopic roentgenograms of the chest A review of the 191 cases constituting the basis of this paper showed that with the use of fluoroscopy and oblique and lateral views, 30 tumors of the thymus were demonstrable an incidence of 15.7 per cent Of the 30 cases in which a definite roentgenologic diagnosis was made, the diagnosis was verified surgically in 17 cases and at necropsy in 5 cases In 8 cases the diagnosis remained unverified, but in these the roentgenographic evidence was unequivocal Furthermore, in none of 19 cases in this series in which the results of roentgenologic examination were negative for tumor were tumors found at surgical exploration (18 cases) or at necropsy (1 case) Only one mistake was made a small tumor was diagnosed radiographically but none was found at operation It is therefore believed that by careful roentgen examination practically all thymic tumors in myasthenia gravis can be diagnosed preoperatively

HAROLD O PETERSON, M D

Congenital Heart Disease with Isolated Inversion of the Abdominal Viscera Paul Forgacs Brit Heart J 9 27-33 January 1947

Forgacs describes two cases of partial inversion of the viscera, with transposition of the abdominal organs only the heart retaining its normal position Both patients showed evidence of congenital heart disease A search through the literature revealed 12 similar cases The author believes that this group may represent a distinct entity, and that the paucity of reported cases is due to lack of appreciation and uncritical reviews of these patients Details of the previously reported cases are furnished

The 14 cases are discussed, but the author hesitates to estimate the total incidence of congenital heart disease or the relative frequency of the various types of cardiac defect associated with isolated inversion of abdominal viscera Predominance of transposition of the atria is, however, striking—8 of the 14 cases demonstrating this rare abnormality Two of the cases had a common atrium supplying both ventricles, and the status of the atria in the 4 remaining cases was indeterminate It would, therefore, appear that this represents the key defect of the heart, and the associated structural changes develop in order to direct arterial and venous blood to their proper outlets Transposition of the aorta to the right ventricle and the pulmonary artery to the left ventricle would achieve this effect All other associated defects are incompatible with normal survival of the affected individual

The author develops an hypothesis based upon the fact that development of the atria is dependent upon the return flow of venous blood from the viscera and placenta in fetal life The flow of blood from transposed viscera to a normally placed sinus venosus, or

lower lobe to extensive involvement of as many as four lobes. Roentgenographic findings range all the way from minimal increase in the prominence of the bronchovascular markings to definite peribronchial thickening and patchy basal pneumonitis. A patient may, however, have negative bronchograms and an apparently normal chest film and yet be partially disabled because of a persistent paroxysmal cough, for roentgen studies can show structural changes when they exceed a certain degree but they cannot demonstrate disturbed physiology of the bronchial musculature and mucosa. The roentgenogram, therefore, is of limited value in chronic mustard gas bronchitis as compared to its role in other chest diseases.

Present routine treatment of chronic mustard gas bronchitis consists of postural drainage, high fluid intake, 60 grains of ammonium chloride daily and removal of the patient from all contact with smoke fumes or dust. Steam inhalations are often of value in easing the tight sensation and wheezing in the chest. Most patients feel considerable relief of wheezing and chest tightness for several days or weeks after a lipidol instillation. Recently good results have been reported with the use of nebulized penicillin.

STEPHEN N. TAGER, M.D.

Surgical Thoracic Tumors in Navy Personnel Wm. Law Watson and Henry D. Diamond. *J. Thoracic Surg.* 16: 1-11, February 1947.

The Naval Hospital in Brooklyn, N. Y., is designated as the regular treatment hospital for neoplastic cases in the Navy serving ships and stations on the Atlantic Coast and in the Ninth Naval District. During a three year period 746 cases of neoplastic disease were seen and treated. Thirty-three of these patients had thoracic tumors suitable for surgery of which 24 were benign and 9 malignant. All the cases were in males, ranging from seventeen to forty-seven years of age. Twenty-three patients had no symptoms and the diagnosis was made by routine chest films. In 5 of these the tumor was malignant.

Of the 33 thoracic tumors 17 were lung tumors including 3 carcinomas and 2 mesothelial sarcomas. There were 3 chest wall tumors of which 2 were malignant and 13 mediastinal tumors. The authors feel that these figures add weight to the growing impression that all persons should have routine periodic chest radiographs.

HAROLD O. PETERSON, M.D.

Carcinoma Simulating Pulmonary Tuberculosis: Differential Diagnosis in the Presymptomatic Stage in Two Cases Louis E. Siltzbach. *Am. Rev. Tuberc.* 55: 170-176, February 1947.

Two cases are reported in which pulmonary neoplasms simulated tuberculosis and the patients were treated for the latter condition for periods of seven and sixteen months respectively, before the neoplastic nature of the lesions was recognized. In both instances the lesions first appeared as moderately well circumscribed shadows about 2 cm. in diameter. Later the shadows became sharper and more distinct. Increase in size was slow. The difficulty in differentiating between early pulmonary neoplasms and small circumscribed tuberculous infiltrates is emphasized particularly when the lesion is situated in an upper lobe. Exploratory thoracotomy is suggested when the diagnosis is equivocal.

L. W. PAUL, M.D.

Pulmonary Adenomatosis Complicated by Lobar Pneumonia Carter M. Alexander and Foo Chu. *Arch. Path.* 43: 92-101, January 1947.

A patient was hospitalized twice for respiratory disease and died ten days following the second admission. At necropsy the lower lobe of the right lung was large, heavy and consolidated. Its parenchyma was yellow pink with a moist gelatinous cut surface. In the lower lobe of the left lung was a solitary nodule with a yellow gelatinous cut surface and a fairly firm consistency.

The histologic examination showed the usual picture of a severe pneumonia in the right lower lobe. In many scattered foci in this lobe there were also alveoli containing tall columnar cells covering the alveolar septa in a single layer. The cells were larger than columnar cells of bronchial mucosa. The nuclei were of moderate size, oval, basal in the cell, abundant in chromatin. The cytoplasm was shown to contain droplets of mucin and there was abundant mucin in the tumor lined alveoli. Many similar foci were also seen in the right upper and middle lobes as well as in the nodule in the left lower lobe. None of the sections showed the columnar cells which lined the alveoli to be continuous with the bronchiolar epithelium. No invasion of blood or lymphatic vessels and no evidences of metastases were seen. The diagnosis was pulmonary adenomatosis.

The authors have reviewed nine other cases in the literature and conclude that the clinical course was not sufficiently typical to make the diagnosis before pathological study. They believe the tumor in their case was of multicentric origin rather than starting in one place in the lung and spreading to other lobes. They also feel that the tumor is benign but potentially malignant. The prognosis is poor. The resemblance to "jagziekte," an infectious disease of sheep in which the alveoli are lined with cuboidal and columnar cells is discussed. In the latter mucin formation is not prominent. The authors believe that the two diseases are unrelated etiologically. (In this connection see also Paul and Ritchie. *Radiology* 47: 334, 1946.—Ed.)

PAUL W. ROMAN, M.D.

Pulmonary Complications of Dorsal Sympathectomy Robert C. Pendergrass and Frank F. Allbritten, Jr. *Am. J. Roentgenol.* 57: 205-212, February 1947.

The authors describe the complications observed radiographically following preganglionic sympathectomies with excision of the proximal segments of the second and third intercostal nerves and division of the dorsal sympathetic chain distal to the third dorsal ganglion. The operative incision is of considerable depth; exposure is consequently limited; thin walled veins are numerous and postoperatively a potentially large extrapleural or intrapleural space results from the dissection. Five instances of resection of the fourth rib and one of resection of the second rib instead of the third were noted. In 3 patients extrapleural hemothorax developed in 2 mediastinal emphysema in 1 massive pneumothorax. Subcutaneous emphysema and small apical fluid levels believed to be due to accumulation of serum or blood or both in the extrapleural space were common postoperative findings.

Routine roentgen examination is recommended following dorsal sympathectomy with postero-anterior and lateral projections with the Potter-Bucky dia-

other members of the staff. The results in the remaining 76 operated cases are tabulated. The embryology, pathology, clinical findings, and roentgen examination are discussed briefly, the major part of the article being given over to a description of the surgical procedures used and the presentation of 2 unusual and 4 typical cases.

Large, Otherwise Normal Gastric Rugae Simulating Tumor of Stomach. A Report of Three Cases. William E Ricketts, Joseph B Kirsner and Walter Lincoln Palmer. *Gastroenterology* 8 123-130 February 1947.

Three cases, well illustrated with roentgenograms and drawings of the gastroscopic findings, show how a gastric tumor may be simulated by large mucosal folds. In 2 of the cases the insufflation of air into the stomach reduced the mucosal folds to normal size. In the other case the subsidence of peristalsis was followed by a return to normal. There was no gastroscopic evidence of gastritis in any of the cases.

[It might well be pointed out that when describing the radiological findings, the authors use the words *contraction*, *peristaltic activity*, and *large mucosal folds*, whereas for the gastroscopic findings they employ the terms *hyperemia*, *edema swollen*. There thus seems to be an attempt to keep certain terms for gastroscopy and certain terms for radiology, whereas actually the two overlap and similar terms could be used for similar appearances. S F T.] SYDNEY F THOMAS M D

Restoration of Gastric Motility by Urethane of B-Methyl Choline After Section of the Vagus Nerves for Peptic Ulcer. Thomas E Machella, Horace H Hodges and Stanley H Lorber. *Gastroenterology* 8 36-51, January 1947.

Two cases are reported in which urethane of B methyl choline was used to promote peristalsis following vagotomy. It appeared to be most effective when given subcutaneously, but oral and sublingual administration in a slightly higher dosage had considerable effect. The action of the drug was demonstrated roentgenologically and by means of balloon-kymographic records.

SYDNEY F THOMAS M D

Gastro-Ileostomy, A Rare Surgical Error. Symptoms and X-ray Findings. Charles H Brown, James R Colvert and Brock E Brush. *Gastroenterology* 8 71-81 January 1947.

The authors found in the literature 23 cases of gastro-ileostomy and to these they add 3 cases of this rare surgical error. Mechanically there are three possibilities when a gastro ileostomy has been done. (1) The gastro ileostomy may be so located and so patulous that the barium is literally dumped into the ileum. Since the stomach is so close to the ileocecal valve the barium is soon in the colon. The resulting clinical features are diarrhea and malnutrition. (2) The stoma may be so located that when the stomach is full, its tonus and the spasm around the stoma permit very little barium to leave the stomach by that route. Instead it leaves the stomach by way of a normally functioning pylorus. Subsequently, when the stomach becomes empty and loses some of its tone the barium, which has now passed through the jejunum into the ileum, may re-enter the stomach through the stoma. This would explain the symptoms of nausea and vomiting with mal-

nutrition and weight loss. (3) There may be a combination of these two mechanisms, part of the barium leaving the stomach through each exit and that which passes through the pylorus partly refilling the stomach sometime later. This would give a combined clinical picture.

The authors' cases illustrate these different mechanisms. In one case all the barium left the stomach by way of a patulous pylorus, only to refill the stomach in five and a half hours. In another case most of the barium left the stomach by way of the stoma, traversed a very short section of ileum to the colon, which was fairly well filled in half an hour. Some of the barium, however, left by way of the pylorus to refill the stomach in three and a half hours. In the remaining case, also, both mechanisms were active.

Refilling of the stomach with barium has not been reported previously. The authors consider it an important diagnostic aid and point out that serial barium films of the whole abdomen should be made whenever a gastro-ileostomy is suspected.

SYDNEY F THOMAS, M D

Post-Bulbar Duodenal Ulcers. Laureano Falla Alvarez and Pedro L Fariñas. *Gastroenterology* 8 1-13, January 1947.

Duodenal ulcer involving the post-bulbar area is not as uncommon as is usually supposed. This report includes 16 cases discovered in a period of five years. The authors point out that other cases may perhaps have been overlooked because of the difficulty of examining this particular area.

The symptoms may be those of the usual duodenal ulcer or may be atypical. When atypical, the pain may begin suddenly and generally mildly increasing rapidly in severity. Food relief is not consistent, and when it does occur is more delayed than in typical duodenal ulcer. The most characteristic radiological sign of post-bulbar ulcer is the niche defect, occasionally *en face* but usually located on the inner border just beyond the bulb. The mucosal folds may appear thick and irregular or cushion shaped and the margins of the duodenum undulant or irregular.

The relative incidence of post-bulbar ulcer as compared to bulbar ulcer in the authors' experience was about one to seventeen. The average age of their patients was forty four years, about ten years more than for the usual duodenal ulcer involving the bulb (cap). Bleeding was the most frequent complication, occurring in 37 per cent as contrasted to an incidence of about 12 per cent in bulbar ulcers.

The literature is reviewed and a good bibliography is appended.

SYDNEY F THOMAS, M D

Intussusception of Excluded Distal Ileum with Spontaneous Expulsion per Anum of Sequestered Intussusceptum. Edward O Finestone. *Surgery* 21 34-42 January 1947.

During the past twenty years, only a small number of cases of spontaneous cure of intussusception by sequestration and extrusion of the invaginated bowel have been reported. Only one case similar to the one here reported is recorded (d'Allaines and Martin. *Arch de mal de l'app digestif* 26 944 1936). In that instance, after exclusion of the distal ileum by ileotransverse colostomy, intussusception of the extruded ileum into the cecum occurred, necessitating resection of the gangrenous portion of the ileum.

from viscera in normal position to a dextrocardia, favors transposition of the atria and the development of congenital heart disease as presented in these cases

LOUIS BERNSTEIN, M D

Diagnosis and Treatment of Tracheal and Esophageal Obstruction Due to Congenital Vascular Ring
Richard H Sweet, Charles W Findlay, Jr, and Gertrud C Reyersbach J Pediat. 30 1-17, January 1947

Two cases of surgical intervention for double aortic arch are presented. Physical signs characterizing the condition include wheezy respiration and attacks of coughing. The stridor is usually noted at birth and often becomes worse during feeding. In many cases the infant breathes normally while asleep. These signs are aggravated by upper respiratory infections, to which these children are unusually susceptible. Dysphagia increases in severity as a more solid diet is given. Stridor may be more pronounced during deglutition, even without dysphagia.

A postero-anterior roentgenogram of the chest may arouse suspicion of anomalous great vessels because of a widened mediastinal shadow extending mostly to the right. Often the normal aortic knob is not seen on the left. The lateral surface of the barium filled esophagus is indented by the aortic arch, which carries the major blood load. The defect can occur on either side. There may be forward and lateral displacement of the trachea and esophagus. Narrowing of the trachea at the site of the constricting vascular ring is a prominent feature.

The first patient described by the authors proved at operation to have a right aortic arch arising from the usual location at the base of the heart. This proceeded posteriorly, joining another much smaller vessel behind the esophagus. The latter (the left aortic arch) arose from the right aortic arch above its cardiac origin. Beyond the junction of the two components, the artery followed the normal course of the descending aorta. Other anomalies found were a left innominate artery and a patent ductus arteriosus.

Embryologically this case can be explained by assuming that the right fourth aortic arch persisted and became the main blood conveyor to the descending aorta. The left fourth arch also remained and thus a permanent vascular ring about the esophagus and trachea was formed.

A right fourth arch was present in the second case also. In this patient the diameter of the vessel was one-eighth that of the aorta. It arose from the ascending aorta above the base of the heart and reunited with the main vessel just below the point where the aortic arch becomes the descending aorta. Another vessel identified as the right innominate artery arose at this junction. Thus a congenital vascular ring was formed by a persistent right fourth arch which connected the ascending and descending aortas.

In the opinion of the authors surgery is indicated when this congenital anomaly is accompanied by symptoms. Perfect results were obtained in the cases reported.

M WENDELL DIETZ M D

Changes in the Precordial Electrocardiogram Due to the Position of the Exploring Electrode
Clough Turnbull Burnett Rocky Mountain M J 44 107-115 February 1947

This is a rather voluminous article, which ought to be of interest to cardiologists, as the author is systematic

scholarly, and thoughtful in the presentation of his material.

He discusses first the inaccuracy of localization of the cardiac apex by the usual methods of physical examination, citing the fact that when patients appear for cardiograms, there has often been considerable disagreement as to just where the apex should be indicated by a marking. Various authors are quoted to emphasize the disagreement as to the most accurate method of localization of the cardiac apex.

As a check on all of the methods, the author has located it fluoroscopically, having an assistant mark the spot with the tip of a uterine sound, then identify it for others by marking with a colored pencil. Using this as a control, the accuracy of the various other methods was appraised. The diaphragm of the fluoroscope should be narrowed greatly. The upright position, standing or sitting is preferred.

The author concludes by saying "Accurate localization of the cardiac apex is difficult or impossible by any method save by roentgen examination. If this is not done frequent and at times significant changes in the electrocardiographic curve may result."

PERCY J DELANO M D

THE DIGESTIVE SYSTEM

Webs and Constricting Bands in the Upper Esophagus (Sideropenic Dysphagia)
Merthyn A Thomas Am J Roentgenol 57 213-219 February 1947

Webs and bands of the upper esophagus are said to occur invariably above the suprasternal notch, the favorite location being the posterocoid area (Macmillan Surg Gynec & Obst 60 394 1935). They are found predominantly in adult women, and from a review of the literature Thomas concludes that the primary cause is a deficiency of iron. The pathological changes in the esophagus as well as such associated changes as splenomegaly, glossitis, cracking in the corners of the mouth, and koilonychia are secondary to a hypochromic anemia.

The radiographic demonstration of the constricting bands or webs is accomplished by a somewhat specialized technic. The site of the obstruction may be demonstrated fluoroscopically while the patient swallows a barium capsule. Detailed study by this method is unsatisfactory however on account of movement due to choking and gagging occasioned by stoppage of the capsule. Films made with rapid exposure immediately after the patient swallows a large mouthful of barium mixture show the constricting band or web in an otherwise distended esophagus.

The treatment consists of dilatation to relieve the dysphagia and large doses of iron continued over a long period of time. The possibility of a relationship between the epithelial changes found in this syndrome and the development of cancer is noted.

Four case histories are included.

ELLWOOD W GOFFREY M D

Esophageal Atresia in Tracheo-Esophageal Fistula
William E Ladd and Orvar Swenson Ann Surg 125 23-40 January 1947

Since January 1939 82 cases of esophageal atresia have been seen at the Children's Hospital, Boston. Four patients were moribund on admission and 2 with multiple associated anomalies were operated upon by

with signs of peritoneal irritation indicative of impending perforation, and the dramatic roentgen demonstration of large ulcerations of the entire colon. Because of the fear of impending complete obstruction which might have necessitated laparotomy, a barium enema was cautiously given to obtain additional information. This roentgen study demonstrated the absence of any obstructive lesion and thus justified the continuation of conservative therapy despite the marked colonic distention. The visualization of unusually extensive ulcers provided an adequate explanation for the severity of the clinical findings. This case illustrates how extensive the disease process in the colon may be in acute ulcerative colitis and still be followed by complete healing within a relatively short time—five months.

A Contribution to the Radiologic Diagnosis of Internal Biliary Fistulas H Plattner J de radiol et d'électrol 27 505-509 1946

The author includes in this discussion the most frequently encountered internal biliary fistula, namely, that produced by ulceration of a gallstone through the gallbladder or common duct into the duodenum, the much less frequent perforation of a duodenal ulcer to involve the biliary tract, and third a traumatic change in the sphincter of Oddi resulting in its incontinence. He covers, also, the operatively produced fistulas in which it has been elected to suture the gallbladder to the duodenum.

The illustrations are typical showing the familiar picture of the biliary tree outlined by barium following a barium meal. There is also a discussion of the outlining of the larger bile ducts by air, which may sometimes be noted in plain films. This phenomenon received abundant emphasis from Rigler some time ago, when he pointed out the need for searching for such bile duct outlines in a scout film for intestinal obstruction.

Although the author does not discuss the physical well being of the patients at great length, this phase of the subject merits a word. If the communication involves only the gallbladder, the symptoms are not apt to be marked, nor is there likely to be a demonstration of the bile ducts by air or barium, but when the communication involves the common duct, the liver receives a liberal dousing with food contents after every meal. Nevertheless, these patients do not seem to show evidence of much biliary infection, and some of them have been followed in various clinics for as long as fifteen to twenty years with internal biliary fistulas unrepaired.

At the gastro intestinal end of the fistula, the duodenum is most frequently involved, the stomach and colon rarely.

The operative mortality is about 10 per cent.

PERCY J DELANO, M D

THE MUSCULOSKELETAL SYSTEM

Hypermobility of Bones Due to "Overlengthened" Capsular and Ligamentous Tissues. A Cause for Recurrent Inter-articular Effusions. Charles J Sutro Surgery 21 67-76 January 1947

Five patients with recurrent effusions of the ankles or knees not associated with known external local trauma exhibited also an abnormal degree of mobility of many joints due apparently to excessive length of the ligaments which stabilize and limit joint motion. This laxity permits repeated damage to the capsular and

ligamentous structures of the joints as a result of minor missteps or subclinical trauma during routine physical activities.

The author describes in detail the range of motion observed in his 5 patients and illustrates his text with photographs and roentgenograms. Practically every joint of the upper and lower extremities and the spine were involved, permitting grotesque positions without discomfort to the patient. Radiographic studies confirmed the abnormal range of movement demonstrated on physical examination.

Treatment of recurrent effusions in such patients should first be conservative, with bed rest and application of cold or warm compresses to the painful part. Traction relieves associated spasm, aspiration is done only if the effusion is large. After cessation of pain, non-weight bearing exercises strengthen the muscles. An elastic bandage may be applied about the joint when effusion has subsided. Permanent use of elastic supports and concomitant muscle training are suggested to prevent further accidents to the unstable joints.

No pathological material is available to determine whether these ligamentous structures contain abnormal amounts of elastic tissue, and the assumption is that the mobility is attributable solely to overlengthening due perhaps to a relative disproportion in rate of growth of adjacent bones and ligaments.

Hypermobility may be a cause of low back pain, cervical rib syndrome, and flat feet and a basis for recurrent subluxation of the intercarpal region, humeral head, or patella. Surgical intervention is indicated in instances of recurrent, protracted disabling frank subluxations of the astragalus, carpal bones, humeral head, or patella with or without hypermobility.

J E WHITELEATHER, M D

Marble Bone Disease. A Study of Osteogenesis Imperfecta. Carla Zawisch Arch Path 43 55-75, January 1947

This is a study of a comparatively rare congenital bone disease known as marble bones, Albers-Schönberg disease or osteopetrosis. The chief histologic characteristics are "an extremely thick cortex of the long and short bones and a narrow marrow cavity filled to a great extent with medullary bone of abnormal structure."

A case described elsewhere in the literature (Windholz Ztschr f Kinderh 51 708, 1931) served for the present study. The infant had died (at the age of thirteen months) since the previous report and the bones were now available for study. Cross sections through the middle of the femoral diaphysis showed the entire history of this bone. The usual normal development of ossification is described in detail by the author and compared with what must have happened in this case. The interpretation of the course of events is based on the microscopic findings observed in cross sections of the femur and ribs. In the femur, the diameter of the marrow cavity corresponded to that of a fetus of five and a half months instead of that of a child thirteen months old. The cavity was bordered by a thick cement line to which endosteal bone had been deposited. Resorption had stopped at the thick cement line.

The findings indicated to the author that marble bone disease starts at the beginning of the second period of bone formation. From then on, pathologic bone tissue is deposited. Resorption of the stratum from within does not take place, and the cortex remains unusually thick. Internal resorption cannot make up for this failure and the entire bone forming process re-

The author presents a detailed summary of the medical and surgical history of a 48-year-old white woman, first admitted to the hospital in 1940 for non-specific ileocolitis of two years' duration. Following medical treatment with unsatisfactory results ileosigmoidostomy was done with division and exclusion of the inflamed distal ileum and cecum. The free edges of the mesentery of the divided ileum were not anchored in any way. During the year following this operation repeated attacks of small bowel obstruction occurred and were controlled with an indwelling Miller-Abbott tube. Finally operation revealed an insinuation of a loop of small bowel beneath the free margin of the mesentery of the ileum just proximal to the anastomosis. The obstruction was reduced and the mesentery was sutured to the posterior parietes. A few weeks after this operation, abdominal pain, distention, fever, and a mass in the right lower quadrant appeared. Shortly thereafter a gangrenous segment of bowel was passed by way of the anus and was presumed to be the excluded loop of terminal ileum.

Subsequent to this spontaneous cure of intussusception, the patient had an intra abdominal abscess and wound infection. Later, operation was required for repair of an incisional ventral hernia at the site of the infection, and in 1943 cholecystectomy and common duct drainage were done but adhesions and the location of these incisions prevented operative confirmation of absence of the distal ileum. At last observation the patient was in a good state of health and free of complaints. Roentgenograms made with barium enema before and after ileosigmoidostomy and before and after extrusion of the intussusceptum are reproduced. The last film shows a small outpocketing of the medial aspect of the cecum which the author believes is all that remains of the distal excluded portion of the ileum.

It is pointed out that when ileocolostomy is done for exclusion of inflamed bowel, the divided mesentery and the terminal ileum should be tacked down to prevent intestinal obstruction due to insinuation of bowel behind the proximal mesenteric edge and intussusception of the excluded ileum. J E WHITEBATHER M D

Residual Defects After Sprue. A Review of 26 Cases. Robert Drew Kendal Dixon and Eric Samuel. *Lancet* 1 129-134 Jan 25 1947.

Twenty six men with sprue who had been inviolated to Great Britain from South East India (25) and North Africa (1) were investigated by clinical, radiological and biochemical means. The body-weight, anemia and appearance of the tongue together with the number and fat-content of the stools were the criteria used for assessing the activity of the condition. On this basis 12 men had completely recovered, 9 showed mild, 4 moderate and 1 severe signs of sprue. The small bowel was examined roentgenologically by contrast media delivered through a Miller Abbott tube. Radiologically 13 men showed no abnormality, this number including 10 who were clinically well, 7 showed mild, 4 moderate and 2 severe changes in the bowel pattern. Radiologic changes were of four types: (1) changes in motility, (2) changes in tonicity, (3) changes in the mucosa and (4) changes in the colon. Roentgenograms showing each type of change are reproduced. Of the 14 patients investigated biochemically only 2 showed definite fat-absorption. In this series it was found that clinical and radiological changes persisted for the same length of time and were of equal value in

assessing the degree of recovery. Deficiency in fat absorption was detectable only in patients showing little recovery.

Steatorrhea. Henry T Ricketts, Samuel N Maimon, and Kathryn Knowlton. *M Clin North America* 31 125-133 January 1947.

Any chronic or intermittent diarrhea characterized by large frothy stools with a 'sour milk' odor suggests steatorrhea. The suspicion can be strengthened by direct microscopic examination of the feces and confirmed by quantitative determination. In fixing etiology the first step is a search for pathogenic organisms in the stools since excessive fat excretion may accompany or follow infectious diarrhea of bacterial or parasitic origin. The next step is a careful roentgen study of the gastro-intestinal tract, including a plain film of the abdomen designed to show pancreatic calculi. If they can be demonstrated, the diagnosis is established at once. If none is found the steatorrhea may be due to (a) other pancreatic disease (obstruction of the duct by radiolucent material, cyst, tumor, or inflammation), (b) disease of the intestines, mesentery or lymph nodes, or (c) 'idiopathic' causes (sprue).

A case of steatorrhea associated with pancreatic calculi, pancreatic cyst, and chronic pancreatitis and one of 'idiopathic' steatorrhea (sprue) are presented, with the differential diagnosis and treatment in each instance. Three cases of steatorrhea due to miscellaneous causes are discussed.

Volvulus of the Caecum. Ralph H Gardiner. *Brit M J* 1 83-86, Jan 18, 1947.

The author, reporting 3 personal cases of volvulus of the caecum, expresses the definite opinion that this condition is far more common than has hitherto been suspected. Non-fixation of the caecum and right half of the colon the only prerequisite, is estimated to occur in from 15 to 25 per cent of all persons, being slightly more common in females though the disease is found more often in males in a ratio of three to one. Partial torsion often occurs in recurrent attacks over a period of years sometimes culminating in an acute complete torsion and may be the cause of obscure abdominal pain and discomfort simulating in some cases subacute appendicitis. The onset of symptoms may be classified as acute, subacute and chronic. In the latter two forms distention is generally gross.

A survey film of the abdomen is of inestimable value and is diagnostic in most cases; the greatly dilated caecum casts a clear shadow which may however, be mistaken for gastric dilatation due to pyloric stenosis. The case history should exclude this error which may arise in cases of slow onset but a small quantity of barium by mouth will indicate the position of the stomach higher up. A barium enema is rarely necessary for diagnosis.

The treatment is surgical, dealing with the condition of the gut found at operation—if viable by derotation and fixation, if gangrenous by right hemicolectomy. ELLWOOD W GODFREY M D

Interesting X-Ray Findings in a Case of Acute Fulminating Ulcerative Colitis. Emil Jobb and Arthur Finkelstein. *Gastroenterology* 8 213-220 February 1947.

The authors report a case presenting an interesting clinical picture of partial bowel obstruction associated

Infantile Cortical Hyperostoses Report of a Case
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Bone & Joint Surg 29 224-226, January 1947

A two month old female infant in July 1945 showed soft tissue swelling over the right scapula, extending into the axilla, with duskeness of the skin over that region. A roentgenogram in September 1945 showed moderate bony overgrowth of the right scapula and later that same month the reaction was shown to have increased, with involvement of the mandible also. Re-examination in October showed considerable extension of the process in the scapula and involvement of the clavicle. Biopsy at this time showed inflammatory change in the muscle. In November the reaction subsided and by April 1946 the bone appeared normal. No definite indication as to etiology is suggested.

JOHN B MCANENY, M D

Syringomyelia, Morvan's Syndrome Edward B Holley J Pediat 30 96-101, January 1947

A case of Morvan's syndrome occurring in a boy of two years and four months is reported. This has been described as a chronic form of syringomyelia characterized chiefly by trophic changes in bones, joints, and skin. The author's patient is believed to be the youngest recorded with this condition. The literature is reviewed, and the 21 cases of the syndrome previously reported are summarized.

Tuberculous Dactylitis in the Adult. A L Umansky, P T Schlesinger and B B Greenberg Arch Surg 54 67-78, January 1947

The authors report a case of tuberculous dactylitis in a 19 year-old Negro male and discuss the differences between adult and childhood forms of this disease. In both age groups the first sign is an elevation of the periosteum with a linear deposit of bone along the diaphysis. An indefinite irregularity of the cortex next appears, and soft tissue swelling soon develops. In the child the periosteal reaction is intense with thickening and expansion of the cortex, the original shaft may be seen enclosed in the new bone. Gradually, however the shaft is destroyed and finally separates as a sequestrum and is absorbed. Pus and sinus tracts form at this time. In the adult, periosteal reaction is lacking. The initial periostitis is replaced by a large area of rarefaction, with absorption of both the fine cancellous and the compact cortical bone. Sclerosis of the neighboring trabeculae may be present. The bone thickens and has a honey-combed appearance. Pathologic fracture often occurs at this stage, at first there is absorption of bone later callus appears and in the end further destruction occurs with debris extending into the soft tissues. The remaining shaft is widened and sclerotic but shows no large sequestrum, involucrum, or fistula formation. The medullary cavity is almost obliterated.

Differentiation from syphilis, enchondroma, malignant tumor, sarcoidosis, coccidioidomycosis, leprosy, and yaws must be made, biopsy is the most reliable guide. Treatment by immobilization and general measures to combat the tuberculous infection usually leads to a good result in childhood and, if operation is indicated, a subperiosteal resection or curettage with or without bone graft often suffices. In adults the prognosis is bad, since disability and recurrent fracture are the rule, amputation proximal to the metacarpophalangeal joint is advised.

Roentgenograms are reproduced showing the progress of the condition over a period of about two years in the authors' case. Amputation was done, with a good result.
LEWIS G JACOBS, M D

Ewing's Sarcoma of Bone Louis Lichtenstein and Henry L Jaffe Am J Path 23 43-77, January 1947

This study, based on 17 cases, 5 of which were autopsied, supports the existence, among the primary malignant tumors appearing in bones, of a tumor entity to which, because of Ewing's pioneer effort to single it out, the name of Ewing's sarcoma should be applied. Beyond the fact that it is a specific malignant tumor primary in bones, and that its cells show no osteogenic potentialities, there is still much to be learned in respect to its histogenesis. Study of the cytologic patterns in this series yields no support for Ewing's contention that the neoplastic cells are derived from capillary or vascular (or perivascular) endothelium. The authors favor a derivation, as suggested by Oberling, from the supporting framework (the reticular tissue) of the bone marrow, a framework which can be regarded as a mesenchymal or primitive form of connective tissue. In viable neoplastic tissue, well fixed and well stained, the type cell is found to have an ill-defined cell border, little cytoplasm, and a fairly large round or oval nucleus showing scattered chromatin.

This series of cases emphasizes the difficulty in making a diagnosis of Ewing's sarcoma by roentgen examination alone. The bone lesion producing the complaints which led the patient to the hospital was often the only lesion discernible even when the entire skeleton was x-rayed on admission. If the amount of bone involvement in the presenting lesion roentgenologically is still small and no lesions are found elsewhere, the picture may be misconstrued as an inflammatory lesion. In most instances, however, the picture suggests a malignant tumor although its exact nature is often misinterpreted.

The only fairly consistent roentgen finding is evidence of lysis of bone, by itself a rather nondescript feature. Thus in some cases the presenting lesion may appear merely as a small zone of mottled rarefaction reflecting destruction of the spongiosa and, to a lesser degree, of the overlying cortex associated with what is as yet only a trace of periosteal new bone apposition in reaction to the neoplastic tissue which has penetrated beyond the cortex. This picture (which may also include some areas of condensation) is very likely to suggest an inflammatory lesion (pyogenic or tuberculous osteomyelitis) rather than a tumor, but within a month or so the roentgenogram shows rapid extension of the pathologic area within and beyond the bone, now strongly supporting a diagnosis of a malignant tumor. Although the film still shows only a relatively small area of bone destruction, this cannot be taken as indicating the actual extent of involvement of the bone, the marrow spaces of which may already be riddled by neoplastic tissue.

When the initial roentgenogram shows rather clearly that the lesion is a malignant tumor, a large area of bone destruction, often with a large overlying soft tissue mass is evident. The affected area in the bone may show distention of its outline but, if present, this is not pronounced. However the affected area appears irregularly rarefied and mottled from the presence of smaller or larger foci of relative radiolucency and shows disruption of the cortical outline over a variable region.

mains disrupted Study of the ribs showed that endosteal ossification undergoes the same pathologic development as the cortical

The author believes the evidence favors an etiology on a basis of a general failure of the fetal bone forming blastema, which becomes evident whenever the bone enters its second period

The x ray findings are explained on the basis of the histologic findings Clubbing of the ends of the long bones, increased density of all of the bones and transverse and horizontal bands of increased and decreased density are seen The clubbing is due to the greater rate of growth at the ends of the long bones The rate of growth is greater at the proximal end of the humerus and at the distal end of the femur

The density of the bones is due to the greater amount of calcium deposited in them The scarcity of fibrils in marble bones, the relatively greater amount of binding substance and the hyperplasia of chondroid bone and basophilic inclusions increase the absolute amount of calcium

The transverse bands of greater and lesser density are an expression of the intensity of longitudinal growth osteoblastic production, and osteoclastic resorption The longitudinal bands are explained by periodic remissions and recrudescences of the pathologic deposition of bone and by periodic recurrences of wide spread resorption These outbursts of resorption even produce osteoporosis, at times leading to fractures of the bones

Microscopic findings from a number of cases from the literature are summarized and references are supplied
STANLEY H MACHT, M D

Sclerosing Osteomyelitis of Garré, with Report of a Case Harold A Lyons U S Nav M Bull 47 83-89 January-February 1947

This is the report of a case that was not diagnosed until persistence of symptoms led to an exploratory operation on the forearm though as the author states the localized pain tenderness x ray picture and absence of constitutional symptoms and of significant laboratory findings should have suggested the true nature of the condition At operation osteomyelitis was discovered and the area was rongeuired down to the depth of the medullary cavity with a good symptomatic result The pathological examination disclosed sclerotic bone with some mild surrounding inflammatory reaction consistent with a diagnosis of chronic sclerosing osteomyelitis Retrospective examination of the roentgenograms which had been regarded as normal revealed a slight area of irregularity on the interosseous aspect of the proximal portion of the radius and the thickened sclerotic bone was then outlined

The roentgen appearance of chronic sclerosing osteomyelitis is typical—increased density with a narrowing of the marrow canal Ewing's endothelioma and osteogenic sarcoma are easily differentiated from this condition Paget's disease may be confusing but is usually multiple with a greater central density and an increase in serum phosphatase Syphilis is excluded by the absence of a history of infection and a negative serologic test Furthermore syphilitic periostitis usually extends over a larger area than was involved in the case here recorded The other two entities to be considered in the differential diagnosis are osteoid osteoma and Brodie's intracortical abscess

SYDNEY F THOMAS M D

A Case of Hypertrophic Osteoarthropathy W B Ayre Canad M A J 56 71-73 January 1947

Ayre describes the case of a 57 year old German prisoner of war in whom all the classical features of hypertrophic osteoarthropathy developed during an eight month period X ray studies revealed a slowly growing mediastinal tumor that responded to roentgen therapy Early changes in the right wrist were described as "irregularities of contour and thickening of the periosteum on the lower end of the radius" The presenting symptoms at the first admission were swelling of the ankles pain in the right wrist and moderate cough with some sputum Clubbing of the fingers developed in the space of one month after hospitalization Symptomatic improvement followed roentgen therapy and some regression of the clubbing and soft tissue swelling in the ankles was observed However, five months later marked hypertrophic changes had occurred—clubbing soft tissue changes, large nails with hyperemic beds deep palmar creases, and enlarged wrists Comparable changes were found in the lower extremities The x ray films of the right wrist revealed a heavy layer of newly formed subperiosteal bone enveloping the distal ulna and radius with irregular subperiosteal proliferation along the metacarpal shafts and proximal two rows of phalanges Changes of similar nature were found in all the bones of the upper and lower extremities with the exception of the terminal phalanges, carpals, tarsals, and bones of the pelvic girdle

Historically the association of pulmonary and cardiac disease with bony and soft tissue changes was first recognized by Bamberger in 1889, and a detailed description was given by Marie in 1890 He labeled the condition pulmonary hypertrophic osteoarthropathy

Ayre discusses the etiology The commonest visceral lesions are pulmonary, either chronic inflammatory or neoplastic but also there are definite associations with cardiac hepatic and gastro intestinal diseases of a chronic nature The changes are more common in males and can occur at any age

The rapid development of the osteoarthritic changes in this case are unusual for bony manifestations are not usually pronounced for two or three years The primary disease process was virtually quiescent during the eight months of observation The mechanism of the development of the hypertrophic changes could not be explained No causal relationships between the primary disease and the secondary osseous changes could be established
WILLIS E MANGES M D

A Rare Osteo-arthropathic Syndrome Radiologic Considerations Franco Fossati Radiol med (Milan) 33 1-14 January 1947

The author describes a case of a generalized condition of the bones and joints characterized by multiple bony ankylosis of the hips elbows knees wrists and ankles accompanied by atrophy and resorption of the distal ends of metacarpals and metatarsals and of the proximal ends of the humeri, radii and ulnae The condition developed over a period of many years, and at the age of forty four the patient was completely incapacitated Excellent roentgenograms of the case are presented the literature is reviewed and the conclusion is reached that this case cannot be fitted into any of the known diseases of the bones and joints

CESARE GIANTURCO M D

Infantile Cortical Hyperostoses Report of a Case D D Dickson, C A Luckey, and N H Logan J Bone & Joint Surg 29 224-226, January 1947

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The reactive deposition of new bone by the periosteum where the neoplastic tissue is penetrating the cortex is certainly not conspicuous. When Ewing's sarcoma involves bones other than long bones, evidence of periosteal new bone apposition, although not uncommon, is not a striking finding.

When the Ewing's sarcoma is located in the shaft of a long bone, the concentric onion-skin layers of periosteal new bone of a laminated pattern held to be so characteristic of the roentgenologic appearance of this tumor are commonly not observed. Rather, a substantial portion of the shaft may show irregular mottled rarefaction, perhaps with complete absence of significant periosteal bone apposition.

Additional lesions found roentgenographically on admission or subsequently like the presenting lesion, show evidence of lysis of bone. They appear first as rather faint, slightly mottled areas of rarefaction. As the resorption of the bone increases, the small, multiple, roundish foci of rarefaction become more distinct and may merge into larger, more clear-cut areas of radiolucency. In flat bones, such as those of the skull or the ilium, multiple, clear-cut, punched-out areas of rarefaction may appear in consequence of lytic destruction of the spongiosa and overlying cortex. Even a neoplastic fracture of a long bone from destructive resorption may become manifest. The actual extent of involvement of the skeleton at any one time is never adequately reflected roentgenologically.

A diagnosis of Ewing's sarcoma on the basis of biopsy should not be made without giving consideration to the possibility that one may be dealing with a sympathetic neuroblastoma or an anaplastic carcinoma metastatic to the affected bone. Such alternative possibilities as primary reticulum-cell sarcoma of bone, Hodgkin's disease, malignant lymphoma, and even myeloma must also be eliminated.

Ewing's sarcoma has a most serious prognosis; all the patients in the authors' series having died. Radiation therapy alone, while often having a remarkable palliative local effect for some time, offers as yet but little hope so far as the ultimate issue is concerned. The combination of radiation therapy and surgery in favorable cases would seem to be more promising but has not yet received sufficient trial.

Sickle Cell Anemia, Case Report with Unusual Roentgen Findings. Ernest Kraft and Giuseppe Bertel. *Am J Roentgenol* 57: 224-231, February 1947.

A case of sickle-cell anemia observed in a forty-three year old colored male is reported. Only a few cases have been reported at so advanced an age. The radiographic changes consisted in demineralization with coarse and irregular trabeculation of the flat bones, biconcavity of the vertebral bodies with trabecular coarsening and porotic areas along with some coarse trabeculation and patchy osteoporosis of the long bones of the lower extremities. The skeletal changes in older patients as exemplified by the present case are different from those seen in early life. In childhood there are usually medullary widening and cortical thinning of tubular bones with possible regression following a crisis. Later in life there are thickening of cortical bone and sclerosis of cancellous bone, coarsened trabeculae being intermingled with patchy osteoporotic areas. The skull is the site of the most frequent changes. Early in life there are thickening of the outer

table and obliteration of the diploic spaces. Fine vertical striations with a "hair-on-end" appearance are seen within and beyond the outer table after the fifth year of life. At a later age the striae are no longer seen and lamellated periosteal new bone formations are found instead.

The question of pathogenesis remains unanswered, as the Rh factor, which now plays such an important role in erythroblastic anemia, has not yet been determined in the survey of families with sickle-cell anemia. So far, sickle-cell anemia like target-cell [erythroblastic] anemia is still considered an entity, being slightly different from the other congenital blood dyscrasias.

ELLWOOD W. GODFREY, M.D.

Anterior Vertebral Wedging—Frequency and Significance. Gilbert H. Fletcher. *Am J Roentgenol* 57: 232-238, February 1947.

The author approaches the problem of anterior vertebral wedging from the statistical standpoint. From lateral roentgenograms of the dorsal and lumbar spine, the height of the anterior and posterior aspects of 3,836 vertebrae were measured and on the basis of these measurements an index of wedging was determined by dividing the height of the posterior aspect of the vertebra by the height of the anterior aspect. For each vertebra the mean index of wedging thus determined and the standard deviation were calculated, and these figures are presented in tabular form. In another table are listed indexes of wedging occurring in 15, 10, and 5 per cent of the vertebrae measured. The figures for the 5 per cent group are held to represent the upper limit of normal, though an index in excess of these is not necessarily abnormal—only on the basis of rarity, probably so. The author concludes that uncomplicated wedging is a symmetrical wedging without the association of other deformities within the limits established in the table is of rather common occurrence and consequently has no clinical significance. With this finding alone one cannot make the diagnosis of a former fracture despite the history of a back injury. In addition, the comparison of the distribution of the index of wedging between groups with backache and without seems to indicate that there is no correlation between uncomplicated wedging and that complaint.

ELLWOOD W. GODFREY, M.D.

Extraspinal Lumbar Meningocele. Robert C. Pendergrass, A. Earl Walker, and John P. Bond. *J Neurosurg* 4: 80-86, January 1947.

Extraspinal meningoceles in the upper lumbar or thoracic region are a great rarity. The authors present a case in a 32-year old Negro complaining of pain in the back and headache upon rapid change of position. On the left side of the back, extending from the 12th dorsal vertebra to the 4th lumbar vertebra, was a large fluctuant slightly tender mass. On coughing the mass distended. Neurological findings were essentially normal. Roentgenograms revealed an absence of the spinous processes of the 11th and 12th thoracic vertebrae and of the left transverse processes of the 1st, 2nd, 3rd, and 4th lumbar vertebrae. The tips of these transverse processes were visualized in the flank at the outer aspect of the mass. In a lumbar myelogram the canal appeared to be normal until the 12th interspace at which point the pantopaque was seen to pass from the left side of the canal through an opening into the large

mass. A diagnosis of extraspinal lumbar meningocele was made. Surgical exposure of the meningocele with an attempt to close the neck was unsuccessful. A partial hemilaminectomy with ligation of the neck of the sac passing through the intervertebral foramen effected a cure.

In this case, the paraspinal lumbar meningocele in all probability was the result of a congenital abnormality of the spine. The localization of the communication between the meningocele and the spinal subarachnoid space by pantopaque myelography made it possible to ligate the neck of the sac through a hemilaminectomy of only two vertebrae. Adequate treatment of such a condition appears to be the obliteration of the communication between the subarachnoid space and the sac. The fluid in the cyst seemed to be more the result of the passage of spinal fluid from the lumbar subarachnoid space into the sac than to the fluid secreted by the sac wall. The patient's complaint of postural headache was the result of rapid changes of intracranial pressure. The mechanism in this instance was probably very similar to that encountered in patients having a large defect of the skull, in whom sudden changes in posture induce headache and vertigo.

Painful, Non-Suppurative, Localized Sclerosis of the Long Bones, with a Report of Two Cases. William Mackenzie. *J Bone & Joint Surg* 29 49-58 January 1947.

The author reviews the outstanding contributions to the literature on sclerosing non suppurative localized lesions in the long bones from the time of Garré down to and including the work of Jaffe and Lichtenstein.

The first of his two cases is that of an eleven-year-old girl with a painful swelling along the medial aspect of the left femoral shaft. This grew larger and more dense. The bone was explored and deeply guttered without discovery of any pus or cavity or sequestrum. Bacteriologic examination was negative and histologic examination showed dense laminated bone without evidence of inflammatory cell infiltration.

The second case reported is that of a fourteen year old boy with enlargement of the middle of the shaft of the left tibia. Early examination by x ray showed chronic osteitis. Two months later dense cortical sclerosis was seen within which there was a radiolucent area. Diagnosis of osteoid osteoma was made. Eight months after the original complaint a large block of bone was removed from the tibia. Histologic examination of this specimen revealed findings that resembled osteoid osteoma as described by Jaffe and Lichtenstein. No positive opinion is expressed regarding the essential nature and cause of the bone lesions in these two cases.

JOHN B McANENY M D

Pathology of Ununited Fractures of the Neck of the Femur. Mary S Sherman and D B Phemister. *J Bone & Joint Surg* 29 19-40 January 1947.

This paper is a review of the pathologic changes seen following ununited fracture of the femoral head. The principal factors which determine union or non union are the extent of the injury, the presence or absence of impaction, accuracy of reduction and fixation, survival or death of the femoral head, and the fact that no periosteal callus is formed. It has been found that pathological changes in the hip joint are rare if the head lives. Its survival depends upon the blood supply. The blood supply to the femoral head is through the anterior

and posterior circumflex arteries and through the ligamentum teres. The femoral head fragment dies if the neck and capsule are completely severed and the round ligament carries no blood supply. In non-union, but with viable head, atrophy will take place but will be equal in both fragments. The head never collapses and the articular cartilage is well preserved. In such cases, union usually follows operative procedure and degenerative arthritis rarely follows.

Femoral neck fracture following irradiation has been studied, showing osteoporosis, sclerosis of the vessel and lack of osteogenesis throughout the fracture area. From roentgenographic appearances it is believed that the head always remains alive. With death of the femoral head, atrophy of disuse cannot occur, but atrophy of the surrounding bone proceeds so that the unaltered femoral head stands out as relatively more dense than the distal fragment. The articular cartilage becomes replaced by imperfect fibrocartilage with subsequent osteoarthritis of the hip joint.

In aseptic necrosis of the femoral head, pathological fracture is prone to occur between the junction of the living and dead bone. Degenerative arthritis is usually present in necrosis of the head with non union but is rarely severe in old cases of necrosis with bony union. With non union there is usually no collapse of a necrotic head but if union occurs and weight is borne, collapse may be expected. Open reduction and fixation of a necrotic head may be followed by bony union and a good functional result may occur but degenerative arthritis usually follows in later years.

JOHN B McANENY M D

Primary Congenital Subluxation of the Hip. Jacques Leveuf. *J Bone & Joint Surg* 29 149-162 January 1947.

French literature distinguishes between luxation and subluxation of the hip. Subluxation differs from true luxation in that the femoral head remains in contact with a more or less deformed acetabulum. Arthrography will help distinguish subluxation from luxation without difficulty even in young children. The prognosis in primary subluxation is grave in most cases because of unsatisfactory reduction and the possibility of resulting osteoarthritis of the hip joint.

In subluxation the limbus is forced upward and inward toward the iliac fossa, in luxation the limbus is forced downward and inward toward the acetabulum. These changes are best seen in arthrograms. The acetabulum in subluxation shows compression and atrophy of the cartilaginous roof probably due to the force of the femoral head against it. In luxation on the other hand the roof and limbus are forced toward the acetabular cavity and the limbus appears hypertrophied producing an hourglass contraction. The characteristic of subluxation and not of luxation is that the femoral head in subluxation is flattened transversely. In luxation it retains its regular contour for a long time. The articular capsule in subluxation is never interposed between the femoral head and acetabulum and the round ligament is practically always absent. In luxation on the other hand the capsule is usually interposed, especially at the lower portion of the cavity. The round ligament is present in about one third of the cases and may even be hypertrophied.

The femoral neck in subluxation is often of the valgus type, measuring 150 to 155 degrees and anteversion is frequently present. In luxation however, no valgus is present and anteversion is only exceptionally encountered.

The author presents a general discussion of the treatment of these two conditions and their complications. Numerous fine reproductions accompany this article.

JOHN B. McANENY, M.D.

Complications of Fractures of the Neck of the Femur H. B. Boyd and I. L. George. *J. Bone & Joint Surg.* 29: 13-18, January 1947.

Three hundred cases of fracture of the femoral neck were reviewed to determine the complications of this injury. The overall mortality was 9.3 per cent. In 141 cases followed for over a year, bony union took place in 122 or 86.5 per cent, with failure of union in 19 or 13.5 per cent. The majority of patients should be followed for at least one year to determine definitely whether bony union will occur. Occasionally, union will occur after a year. In 10 fractures, poor reduction, inadequate mechanical fixation, premature removal of the nail, or a combination of these factors contributed to non union. The remaining 9 were satisfactorily reduced and fixed but non union nevertheless occurred. In 2 of these cases Paget's disease was present in the head and neck of the femur.

Aseptic necrosis of the femoral head occurred in about 33.6 per cent of patients and was demonstrated within two years of the fracture. Arthritic change in the joint was demonstrated in 33.6 per cent of the patients. Aseptic necrosis and arthritic change occurred coincidentally in some instances.

Final analysis of this group of patients shows that a mortality of about 9.3 per cent may be expected in fractures of the femoral neck, poor end result in 28.1 per cent, which includes ununited fracture and severe arthritic change, fair end result in 19 per cent, and good end result in 43.6 per cent.

JOHN B. McANENY, M.D.

Fracture-Dislocation of the Ankle with Fixed Displacement of the Fibula Behind the Tibia David M. Bosworth. *J. Bone & Joint Surg.* 29: 130-135, January 1947.

In December 1944 the author encountered a fracture-dislocation of the ankle in which attempt at closed reduction produced a poor result with failure to maintain reduction. Exploratory operation was done at which time it was found that the proximal portion of the fibula had been displaced behind the tibia and was caught back of the posterolateral ridge of that bone. It required considerable force to separate and pry the fibula loose from the ridge of the tibia but after this reduction of the fracture-dislocation was easily secured. Several additional cases were later encountered in which this same situation was found.

Roentgenographically the posterior location of the proximal fibular fragment can usually be demonstrated especially in the lateral view if this condition is watched for and expected in fracture-dislocation of the ankle. Open reduction is necessary and extreme force is required to separate the proximal fibular fragment from the tibia.

JOHN B. McANENY, M.D.

GYNECOLOGY AND OBSTETRICS

Recognition of Midpelvic Contraction William C. Eller and William F. Mengert. *Am. J. Obst. & Gynec.* 53: 252-258, February 1947.

Midpelvic contraction may be recognized more frequently, in the authors' opinion, if roentgen mensuration is employed in the presence of anyone of the following:

- A. History
 - 1. Difficult labor especially midforceps delivery
 - 2. Unexplained stillbirth
- B. Palpation
 - 1. Prominent ischial spines
 - 2. Sacral deformity especially forward angulation
- C. Manual mensuration
 - 1. Inlet
 - a. Ability to touch sacral promontory on vaginal examination
 - b. External measurements below average, i.e. interspinous 23 cm or less, intercrural 26 cm or less, external conjugate 17 cm or less
 - 2. Outlet
 - a. Bisischial 8.5 cm or less
 - b. Sum of bisischial and posterior sagittal 15.0 cm or less
- D. Non engagement of fetal head at term in a primigravida

Hand in hand with a high index of suspicion of midpelvic contraction and equally important to the obstetrician is the conviction based on office methods that a given pelvis is normal. With average inlet measurements (intercrural 29 cm, interspinous 26 cm, internal conjugate 20 cm) inability to touch the sacral promontory on vaginal examination, average outlet measurements (bisischial 9.5 cm +) and no palpatory findings or obvious history as enumerated above, the obstetrician is justified in concluding that no serious midplane contraction exists. In such patients roentgenologic mensuration is unnecessary.

Oil Embolism Following Hysterosalpingography Francis M. Ingersoll and Laurence L. Robbins. *Am. J. Obst. & Gynec.* 53: 307-311, February 1947.

The purpose of this report is to record another instance of oil embolism, a serious complication following hysterosalpingography. The literature on the subject is reviewed by the authors and a fatal case is mentioned (Gajzágó, *Zentralbl. f. Gynäk.* 55: 543, 1931). The case reported is that of a 43-year old woman with oil emboli to the lungs following the injection of 8 cc of iodized oil one day following cessation of the menstrual period. The initial uterosalpingogram showed oil in the pelvic veins. Symptoms developed on the day following the injection of the oil and roentgenograms of the chest showed patchy areas of increased density consistent with infarcts. The patient had a slight elevation of temperature for four days following which it returned to normal. There was no recurrence of pulmonary symptoms and films obtained just before the patient's discharge from the hospital showed considerable improvement in the appearance of the chest. Several precautionary measures are suggested by this case. Uterosalpingography should not be done until

eight to ten days following operation on the uterus or following the cessation of menstruation. After the injection of 2 c.c. of oil a film should be taken to determine whether any oil has entered the pelvic veins. Care should be taken to use a blunt-tipped cannula, thus causing as little direct trauma to the endometrium as possible. It is quite important that close co operation between the roentgenologist and gynecologist be maintained in order to prevent intravasation of oil into the uterine vascular channels. MORRIS IVKER, M.D.

Uterosalpingography Report of a Fatality Arthur M. Faris and Allen McMurrey. Texas State M. J. 42: 592-597, February 1947.

The authors present a series of illustrations demonstrating the usefulness of uterosalpingography. They use lipiodine in preference to any of the heavier oils, as lipiodol, skiodan, acacia, etc., because of its more rapid absorption and less irritative properties. The procedure should not, however, be considered entirely harmless, and certain precautions are suggested in its performance. The contrast medium should be injected slowly and the amount limited to the minimum necessary to demonstrate the pathologic condition, usually 5 to 6 c.c. Anesthesia is rarely indicated and should be avoided.

A fatality following uterosalpingography occurred in the experience of one of the authors. The patient was given light cyclopropane anesthesia, because of pain associated with the procedure on an earlier occasion, and 12 c.c. of lipiodine were injected readily. Stereoscopic roentgenograms were taken and the cannula through which the injection was made was removed. Death ensued within fifteen minutes. The films of the uterus and surrounding area showed the filling of venous plexuses bilaterally with the opaque medium. Its intravenous course is clearly evident in the reproductions.

The authors believe that the intravasation of the medium into the veins was probably the result of injury to the cervical canal by the cannula, though the anesthesia may have played a role. The possibility of embolism as a cause of death is believed to have been fairly well ruled out by postmortem studies on both lungs and skull. Unfortunately necropsy was not performed. The most probable explanation of the fatality is considered to be a sudden reaction to the iodized oil. It is felt that the patient may have been sensitized by the earlier injection to such an extent that the second amount proved fatal when it entered the blood stream.

SYDNEY J. THOMAS, M.D.

THE GENITO-URINARY SYSTEM

Nephrolithiasis in Skeletal Affections A. Schüpbach. Schweiz. med. Wchnschr. 77: 76-79, Jan 11, 1947.

The author points out that there are two types of urinary lithiasis: that due to infection and that due to hyperexcretion of calcium salts. This latter type may occur whenever very active calcification of bone is taking place, as in severe multiple fractures, especially those resulting from war wounds. The relationship between von Recklinghausen's disease, hyperparathyroidism and nephrolithiasis is well known. Albright's dictum that renal symptoms may occur in the absence of skeletal changes is emphasized. Other diseases such as

bone or joint tuberculosis, multiple myeloma, or hypercalcemia may result in a similar hyperexcretion of calcium in the urine. Five cases are reported, two of von Recklinghausen's disease and one each of visceral sarcoidosis with generalized skeletal foci, of extreme primary osteomalacia, and of symptomatic sprue resulting from gastric resection. All of the patients showed kidney stones due to hyperexcretion of calcium.

LEWIS G. JACOBS, M.D.

Certain Urographic Figures: Precapillary Shadows (*Images en boule*) and the Kidney Shadow R. Hickel. J. de radiol. et d'électrol. 27: 509-515, 1946.

The principal emphasis of this paper is upon watching pyelograms for a visualization of the caliceal tip in the absence of the usual visibility of the infundibulum. The mechanism of this phenomenon is gone into in some detail and the hydrostatics of the situation are made clear. The resultant clinical fact is that varying degrees of obstruction below the kidney pelvis produce a visualization *en boule*. Back pressure of urine dammed above a ureteral stone or kink or other obstruction prevents free urinary secretion, hence, the dye is held back, and only the caliceal tips are brought into relief. In the presence of such shadows on one side, or both, the logical route of inquiry is in the direction of discovering a ureteral obstruction, even though no evidence of such has been hitherto apparent.

When there is no back pressure in the kidney pelvis, the outline of the kidney parenchyma is not likely to be so sharp, since urine escapes freely from the kidney, fills the infundibula without hindrance, and the *images en boule* are no longer sharply evident for lack of contrast.

PERCY J. DELANO, M.D.

Spinal Cord Injuries: Urethrographic Studies of the Bladder Neck George C. Prather and Boris Petroff. J. Urol. 57: 274-284, February 1947.

Material for this paper was accumulated at two Army hospitals in the United States that were designated as centers for men with spinal cord injuries. The object was to record the anatomical status of the bladder neck in such patients. Observations were made in 129 cases.

Two methods of urethrography were employed. The urethrograms reproduced in the paper were obtained following retrograde injection from the external meatus with 25 to 30 c.c. of opaque medium and represent a resting urethra.

In 36 of the cases there was complete transection of the spinal cord or cauda equina, and in 30 of these there was some dilatation of the bladder neck. Among the 93 patients with partial transection there were 65 with some dilatation or relaxation of the bladder neck. None of the patients was seen within as short a time as four weeks following injury and in most cases two to four months had elapsed. Even so, the time factor showed an appreciable effect on the observations, especially in cases of complete transection of the cord. Of 8 such patients examined within three months after injury, 3 showed normal urethrograms and 5 presented some evidence of dilatation. In a similar group of 28 men whose initial urethrographic examination was made four to twelve months after injury, only 3 had no dilatation of the bladder neck. In cases of partial transection the time element appeared less impressive.

The cases are further considered according to the level of the injury. There were no cases of complete transec-

tion of the cervical portion of the cord. Of the 10 patients with partial cervical transection 6 showed dilatation. Complete thoracic transection occurred in 29 cases, and the ratio of dilated to normal bladder neck in this group was almost 4 to 1. With partial thoracic transection there was a much higher percentage of normal findings, 12 out of 29. All patients with complete cauda transection had dilatation of greater or lesser degree. Even in partial transections of the cauda the patients with dilatation numbered 3 1/2 times as many as those with normal findings.

It appears that dilatation of the bladder neck is predominant but not constant in those with complete transection of the spinal cord, and that the same finding is always present in complete transection of the cauda equina. In those with partial transection dilatation of the bladder neck is common and occurs with increasing frequency from the level of the cervical region to the cauda equina.

JOSEPH P. TOMSULA, M.D.

Venous Invasion Due to Urethrograms Made with Lipiodol. E. Granville Crabtree. *J. Urol.* 57: 380-389, February 1947.

Although venous invasion has been reported in connection with pyelography, uterosalpingography, and less commonly with ureterography, there appears to be no mention in the American literature of invasion of the venous channels demonstrated roentgenographically following urethrography. Clinically venous invasion has been suggested by 'catheter chills' indicating septicemia and by sudden deaths from cocaine and other anesthetics used in the urethra.

A total of 27 cases of venous invasion from urethrography demonstrated by x-ray were collected from the European literature. Edling (*Acta radiol. Suppl.* LVIII, 1945) found it 15 times in a series of 570 cystourethrograms. Among the 27 collected cases there were 4 deaths, due to emboli from oily media and thorium. Death from fat embolism may be instantaneous or delayed for a few days, and is dependent on the region in which the embolism occurs. In some instances no harm results, the oily medium, when it reaches the veins or lodges in the tissues, disappears slowly, in weeks to months. Thorium is especially contraindicated, as it is a tissue irritant and remains permanently.

An important consideration in determining the readiness with which the veins are entered from the lumen of the urethra is the great vascularity of the organ and the thinness of the lining. When the urethra is distended the mucosa has a thickness of only 2 to 3 thin flat cells. A survey of the reported cases reveals that permeation of the veins can occur either from the use of undue force from without during injection or from force supplied by the bladder and abdominal

muscles in voiding against obstruction in the urethra. The phenomenon is more likely to result when urethrography is done on patients with acute urethritis after injury, and after instrumentation.

There does not appear to be any close relation between the amount of medium injected, discomfort produced during injection, or bleeding caused by the injection and the occurrence of venous invasion. In most of the cases in which the phenomenon occurred there was no discomfort and x-ray alone demonstrated the dye in the veins.

Apparently the veins may be patchily filled and incompletely outlined by the opaque medium, and as a result can easily be missed or misinterpreted when the phenomenon of invasion does occur.

A case of venous invasion following urethrography with roentgenographic illustrations is fully reported by the author.

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X-Ray Exposure Meters and Automatic Exposure Timers. L. M. Garrett. *Texas State J. Med.* 42: 597-602, February 1947.

This is a down-to-earth, simple interpretation of the highly complicated mechanism of the exposure meter and the automatic exposure timer which should be read by everyone not understanding their principles and uses. The exposure meter is an electronic device based on a photoelectric cell which is used to ascertain the correct setting of the x-ray machine for making the actual roentgenogram. The automatic exposure timer, on the other hand, is incorporated in the x-ray equipment and cuts off the x-ray when the correct exposure is made. The electronic devices which are used to perform these tasks are explained in some detail which is well within the comprehension even of one not skilled in electronics.

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L. W. PAUL, M.D.

RADIOTHERAPY

General Factors in Irradiation Therapy. Curtis F. Burnam. *Ann. Otol. Rhin. & Laryng.* 55: 764-778, December 1946.

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improvement or complete return of hearing follows, and in many cases the bluish discoloration of the tympanic membrane also disappears

Of repeated attacks of eustachian tube obstruction are a common cause of impaired hearing in children. Repeated examinations, for research purposes, of 1,365 unselected public school children showed that adenoids recur in more than 75 per cent of those whose tonsils and adenoids have been removed before puberty. Nearly 40 per cent of these had either impaired hearing for high tones alone or for all tones in the speech range. In addition to loss of hearing, the regrowth of lymphoid tissue after operation predisposes to recurrent upper respiratory infections, attacks of suppurative otitis media, sinusitis, and bronchial infections. For several years the author has supplemented every tonsillectomy with irradiation of the nasopharynx. The first treatment is given about two weeks after the operation, and two additional treatments are given at intervals of two weeks. With the 50 mg. monel metal applicator, the dosage for all treatments is eight and a half minutes on each side.

Operative removal of very large adenoids followed by a series of radium treatments, is always more satisfactory than irradiation alone, because of the mechanical difficulty of applying adequate irradiation to a large mass in this area with the nasopharyngeal applicator. It is decidedly dangerous to plunge the applicator into the mass of adenoids, to bend the applicator, or to construct it with a hinge so the angle of the radium-containing chamber may be changed. This introduces a hazard that the radium-containing part may some day break away and be swallowed or aspirated. If the adenoids are relatively small, however, and it is possible to introduce the applicator far enough into the nasopharynx to permit sufficient irradiation of the tubal orifices, the fossa of Rosenmüller and the lateral walls, then operation is not necessary.

The radium applicator should not be used in the nose itself for any condition except nodules of lymphoid tissue. Polyps are extremely resistant, and the applicator is not suitable for the treatment of malignant growths. It was designed for one purpose alone—the removal of lymphoid tissue.

During the war approximately 25,000 treatments were given with the monel metal radium applicator by medical officers of the Army Air Forces and at the New London Submarine Base, in order to prevent recurrent aerotitis and thus conserve manpower. The average result was 90 per cent effective. Not a single instance of radium burn or radium poisoning, with a drop in the white count, has been reported. The author has given treatments with the nasopharyngeal applicator almost daily for twenty years and has suffered no ill effects. The only requirements are an accurate examination with the nasopharyngoscope to establish the indication for radium treatment, placing the applicator so that the side, not the end, of the radium-containing chamber is in contact with the tissue to be treated, and finally the greatest care to time each treatment accurately.

Precautions for the protection of office personnel are included. It is of the utmost importance for the radium to be stored and the treatments to be given at least 20 feet from those who are daily exposed to its effects. The two-inch lead cylinder that comes with the applicator is intended to make transportation practicable, but for storage in an office the lead should be at least 6 inches in thickness.

STEPHEN N. TAGER, M.D.

Mechanism of Radiation Effects against Malignant Tumors. Shields Warren. *J. A. M. A.* 133: 462-463, Feb. 15, 1947.

The author presents a brief discussion of radiation effects on malignant tumors. One of the important ways of influencing growth, both normal and abnormal, is by radiation. It is the radiant energy absorbed by the tissue or cell that is effective, not that which is delivered to it. All types of ionizing radiations—the roentgen ray, the gamma ray, the alpha particle, the beta particle, the neutron—have essentially the same qualitative effects on cells exposed to them, so far as can be determined by histologic examination.

The first noticeable effect on cells is interference with mitosis, which is closely followed by vacuolization and swelling of the cytoplasm. Later pyknosis and autolysis of the injured cells take place. Partial or complete recovery of some of the tumor cells occurs, and were it not for secondary effects on the connective-tissue stroma and blood vessels, no lasting effects on an irradiated part would be noted. Fibrous tissue and hyaline act as barriers to metabolic exchange of tumor cells and hinder their spread.

The law of Bergonié and Tribondeau, according to which the radiosensitivity of cells is in inverse ratio to their degree of differentiation, while holding true to some degree, has many exceptions. Tumors which regress with a dose of irradiation that does little harm to adjacent tissues, up to 2,500 r, may be called radiosensitive. Radioresponsive tumors are considered as those which regress with dosage of 2,500-5,000 r, with adjacent tissue harmed to a moderate degree. Radio-resistant tumors are those which do not respond any better than adjacent normal tissue. Radiosensitive tumors are not necessarily radiocurable.

Radioactive isotopes, particularly of phosphorus and iodine, which are absorbed selectively to some degree, make possible irradiation of tumor cells without too much injury to normal cells. JOSEPH HANELIN, M.D.
(University of Michigan)

Limits of Roentgen Therapy of Cancer. A. Rosselet. *Schweiz. med. Wchnschr.* 77: 106-107, Jan. 11, 1947.

A very general discussion, containing nothing new, of reasons for the lack of material improvement in the results of radiation treatment of cancer in the last few years. Special emphasis is placed on radiosensitivity and "our ignorance of methods which would permit us to change cellular radiosensitivity, to increase its amount, in other words, to transform a radio-resistant cell into a radiosensitive cell more vulnerable to the actions of radiations. And we do not see in other sciences, as chemistry or biochemistry, capabilities of giving us a solution to this problem—if there is one!"

LEWIS G. JACOBS, M.D.

Cancer of the Eyelid Treated by Radiation, with Consideration of Irradiation Cataract. Howard B. Hunt. *Am. J. Roentgenol.* 57: 160-180, February 1947.

From a critical study of 100 selected cases of cancer of the eyelid the author forms the opinion that the treatment of choice is fractionated roentgen therapy. The eyeball and lens can be effectively protected against superficial roentgen rays and beta rays by an eyeshield equivalent to 1 mm. of lead. No eyeshield is adequate for protection against the more penetrating gamma rays of radium. In a fifteen year period of observation 4 of

tion of the cervical portion of the cord. Of the 10 patients with partial cervical transection, 6 showed dilatation. Complete thoracic transection occurred in 29 cases, and the ratio of dilated to normal bladder neck in this group was almost 4 to 1. With partial thoracic transection there was a much higher percentage of normal findings, 12 out of 29. All patients with complete cauda transection had dilatation of greater or lesser degree. Even in partial transections of the cauda the patients with dilatation numbered 3 1/2 times as many as those with normal findings.

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cludes with some general principles of the application of these agents in ophthalmology and otolaryngology. The second takes up the irradiation of the nasopharynx with the aid of a special radium applicator (see Burnam and Crowe, *Mississippi Valley M. J.* 67: 109, 1945; *Abst. in Radiology* 47: 208, 1946) for the destruction of excessive lymphoid tissue which is so frequent a cause of deafness. Under this treatment the lymphoid tissue around the tubal orifices gradually disappears, marked

cures In Stage III the primary growth is of indeterminate size with unilateral operable cervical nodes Thirty cases were so classified, with 7 or 23 3 per cent five year cures In Stage IV the primary growth invades surrounding structures with inoperable cervical metastases Twenty-eight cases belonged in this group with 1 or 3 6 per cent five-year cures One of the most important factors in every respect—diagnosis, therapy, and prognosis—is the presence or absence of metastatic involvement of cervical lymph nodes

In the treatment of the primary lesion, surgery has been replaced by irradiation Whenever possible, intracavity treatment cones are used perorally, while external fields of irradiation are employed only as a supplement or when the site of the lesion cannot be reached by a peroral cone Whether the radiation is administered exclusively through the oral cavity, or whether supplementary external fields are used, a daily dose of 400 r in air is considered desirable, the total dosage being 4,000 to 4,800 r, depending on the size of the cone This is delivered with 200 kv, 15 ma, and with a Thoraeus filter equivalent to 2 0 mm of copper Target to skin distance is 25 cm for the intra oral cone and 50 cm for external irradiation Radium needles are implanted on the last day of roentgen therapy for an average exposure of 1,200 mg-hr in the anterior two thirds of the tongue and 800 mg-hr at the base The 1,200 mg-hr amount to 4,800 gamma roentgens for a lesion 2 5 cm in diameter and a volume of about 8 c c this would be equivalent to approximately 4 8 erythema doses If it is assumed that the tissue exposure at the base of the lesion corresponds to 75 per cent of the roentgen exposure in air, it would average about 3 600 'tissue roentgens' or roughly 5 2 erythema doses Adding these two biological values of exposure the total is found to be in the neighborhood of 10 erythema doses With interstitial needles rather than radon seeds, radiation necrosis is less frequent, the result is less painful and it has not been found necessary to remove the growth as has been unavoidable in the case of radon seeds

Palliative treatment also begins with roentgen therapy By peroral administration a total dose of 4 000 r in air usually proves sufficient to remove radiating as well as local pain An external portal is used exclusively in those cases where it is possible to aim the radiation through cervical nodes into the primary growth Immediately afterward interstitial irradiation by means of radium needles is instituted A cancerous growth involving one half of the tongue will require 1 500 to 1 600 mg-hr while in more extensive lesions 2 000 mg-hr may be needed These doses will permit a possible repetition of interstitial irradiation while roentgen therapy may also be repeated after an interval of three months

Radical neck dissection should in no case be undertaken earlier than two or three weeks after the treatment of the primary lesion has been terminated If by that time it is evident that the lingual growth has been responding satisfactorily to radiation therapy neck surgery can be undertaken provided all of the following conditions are fulfilled (1) the general condition of the patient warrants (2) the life expectancy is weighed against the statistical surgical risk (3) cervical nodes are considered as operable only if the primary lesion has not transcended the midline and has on the basis of primary growth biopsy proved to be of only limited malignancy (4) the secondary metastatic involvement

has remained unilateral, (5) the node—or nodes—is movable and shows little evidence of invasion An irregular outline of a metastatic node, or its partial fixation, indicates that the involvement has extended beyond the capsule and in such cases dissection would lead to contamination of the operative field and to subsequent recurrence

Where radical block dissection is not feasible, interstitial irradiation supplements more extensive roentgen therapy
ELLWOOD W GODFREY M D

Carcinoma of the Breast. Karl F Kesmodel
South M J 40 43-46, January 1947

An analysis of the cases treated by the author for a five year period between 1936 and 1941 is presented It is again emphasized that the survival rate is greatly reduced when the axillary nodes are already involved by the carcinoma when the patient comes to surgery Radiation is stressed as an important therapeutic agent in the relief of pain from bone metastases The value of castration as an adjunct in therapy remains questionable The author refers to the work of Adair and Herrmann (Ann Surg 123 1023, 1946), who used testosterone propionate in the treatment of 11 patients 4 of whom exhibited a favorable response None was used in the present series

The author's routine method of prophylactic post-operative x ray therapy is described If for any reason surgical treatment cannot be undertaken in a patient who is considered 'surgically curable,' roentgen therapy is instituted

Radiation sickness the most frequent complication to therapy, is treated by a combination of thiamin hydrochloride and pyridoxine hydrochloride, 50 mg of each per c c of solution One cubic centimeter, intravenously or intramuscularly, on alternate days is usually sufficient

The author urges the consideration, treatment, and care of the so-called 'incurable' cancer patients in view of the fact that their lives can be prolonged and their pain can be relieved
MORRIS IVKER, M D

Lymphosarcoma of the Bladder, with Brief Review of the Literature Benjamin Levant and Richard E Rosenfield Urol & Cutan Rev 51 6-9 January 1947

Primary lymphosarcoma of the bladder is a rare neoplasm It was first reported in American literature in 1942 by Kreutzmann (J Urol 48 147 1942) There have been seven cases in all reported in the literature since 1835, exclusive of the one here recorded, and pertinent details of these are tabulated The symptomatology of this disease is similar to that of any other tumor of the bladder pain, hematuria and urinary retention The diagnosis is made by means of cystoscopy cystograms and microscopic studies The best results have been obtained by resection followed by irradiation

The author reports a case of primary lymphosarcoma of the bladder which appears to be of the reticulum-cell type Treatment was by resection followed by radiation therapy and at the time of the report less than a year after operation the patient was without evidence of recurrence
MAURICE D SACHS, M D

Radiotherapeutic and Radiosurgical Indications in Cancer of the Rectum R Mathey-Cornat J de radiol et d electrol 27 533-536 1946

This article on cancer of the rectum, rather than presenting any new departure in treatment or even a de-

the 100 patients died from cancer of the eyelid. Therapeutic failures result from (a) advanced and inaccessible disease, (b) impairment of the tumor bed by prior inadequate therapy, (c) insufficient or uneven doses, (d) incomplete marginal coverage of lesion, and (e) inadequate follow up of patients.

Histopathology. Biopsy was done in 70 of the 100 cases. Basal-cell carcinoma constituted 70 per cent of the neoplasms, squamous-cell 15 per cent mixed squamous-cell and basal cell, or keratinizing basal-cell lesions 5 per cent, with the more benign lesions such as keratotic horns and papillomas making up the remaining 10 per cent. Biopsy is occasionally foregone to minimize scarring.

Distribution, Extension, and Metastases. Forty eight per cent of the lesions occurred along the lower lid and 34 per cent above the inner canthus with only 6 per cent along the upper lid and 12 per cent adjacent to the outer canthus. Extension is primarily by direct infiltration with occasional extensive subcutaneous progression of basal cell lesions or local permeation along adjacent lymphatics with the production of what appear to be multiple foci. Lymphatic penetration of the orbital fascia may give rise to intra-orbital metastases with pain and proptosis. Lesions about the inner canthus tend to invade the lacrimal duct, with occasional ulcerative invasion into the ethmoid sinuses. Squamous cell lesions may metastasize to the regional nodes. The superficial and deep lymphatics from the lateral three-fourths of the upper lid and the lateral aspect of the lower lid drain laterally into the superficial and deep parotid nodes just in front of and below the ear. The medial group of lymphatics drain the region of the inner canthus and the medial three-fourths of the lower lid, and follow the course of the facial vein down into the submaxillary group of nodes.

Effect of Irradiation on the Eye. Conjunctivitis precedes epidermitis of the skin by three to five days. The eyelashes are lost from the irradiated area after ten to twenty days and have not returned in areas successfully treated for cancer of the eyelid. The crystalline lens is very susceptible to irradiation injury although a period of three months to twelve years may elapse before cataract becomes apparent. It now seems well established that the primary mechanism of irradiation cataract is direct injury to the subcapsular epithelial cells along the anterior aspect of the equator of the lens. Eighty-eight per cent of gamma radiation from radium passes through 2 mm of lead and 83 per cent through 3 mm of lead. A 1 mm lead shield will absorb 99+ per cent of x radiation energized by 80 kv without filter, and 97+ per cent of radiation energized by 140 kv filtered through 0.25 mm of copper and 1 mm aluminum, according to the author's measurements.

Radiotherapy. Roentgen therapy has become the radiotherapeutic method of choice due to its proved effectiveness, accuracy, simplicity and restriction of exposure more closely to the diseased area. The larger the lesion in extent the more advisable fractionation becomes, in order to preserve the health and nutrition of the tumor bed. Fractionation is also advantageous in lesions over 3 or 4 mm in thickness since shrinkage of the tumor following initial exposures permits more effective exposure of the base of the cancer with relatively less irradiation of underlying tissues. Inasmuch as roentgen dosage on small lesions is usually recorded in air without back scattering, it is essential to bear in mind that air dosage must be increased about 10 to 50

per cent when dealing with lesions less than 10 to 5 mm in size in order to deliver dosage comparable to that developed in a lesion 20 to 30 mm in size.

With a single roentgen treatment, an average dosage of 2,875 r in air was found effective. An average dosage of 3,400 to 4,200 r in air was employed when two treatments were delivered within a period of two to seven days. A total dosage of 4,500 to 5,400 r in air was employed when three treatments were delivered within a period of three to fourteen days. A total dosage of 5,000 to 8,500 roentgens was employed if five or more equal treatments were delivered during a period of five to twenty-one days. In general this method proved effective in eradication of cancer of the eyelid with maximal preservation of the uninvolved tissues and with minimal injury to the eye when it was properly protected by an eyeshield.

ELLWOOD W. GODFREY, M.D.

Radiotherapy of Epitheliomas of the Eyelids. F. Bælesse, M. Dollfus, A. Ennuyer, and J. Reverdy. *J. de radiol. et d'électrol.* 27: 515-526, 1946.

This article contains a comprehensive description of malignant lesions of the eyelid, classifies them histologically, and gives end results of treatment. In general, the authors use lead shields (external) and retract the affected portion as much as possible. Sometimes, when using very high intensity radiation, where the time will be short, they rely somewhat upon the patient, who is instructed to keep his eye rotated to a fixed point, thus tilting it out of border radiations.

Most of the ocular complications observed by the authors have followed the use of radium plaques; they have had the least trouble with the Chaoul type of instrument. The article includes a complete discussion of the complications of treatment by the attending ophthalmologist who takes up the injuries (which have been slight and infrequent) in order and discusses their prevention.

This is a most worthwhile article and is recommended to all who have found treatment of eyelid lesions beset with difficulties.

PERCY J. DELANO, M.D.

Cancer of the Tongue. George S. Sharp and Harold D. Spickerman. *Am. J. Roentgenol.* 57: 181-198, February 1947.

The authors analyze 81 unselected consecutive proved cases of cancer of the tongue. Twenty-seven patients were seen in private practice and 54 at the Veterans Administration Facility, Los Angeles. It is felt that leukoplakia concomitant with lingual carcinoma favored successful treatment, as the growth is usually slow and of a low degree of malignancy while the tendency to invade adjacent tissues or to metastasize to cervical nodes is less pronounced. On the other hand, a highly inflamed growth associated with ulceration is locally aggressive and metastases are the rule. Still another course is characterized by moderate local growth and early massive metastases to the cervical nodes.

A classification is proposed which indicates the condition of the primary lesion and the presence and extent of secondary involvement. Stage I consists of a primary growth less than 1.5 cm in diameter. Nine cases fitted into this category with 5 or 55 per cent five-year cures. Stage II comprises 14 cases with the primary growth less than 3 cm diameter and 7 or 50 per cent five-year

Radiation Therapy for the Removal of Adenoid Tissue Donald F Proctor Arch Otolaryng 45 40-48, January 1947

This is a further report of experiences at the Hagerstown (Maryland) Clinic for the treatment of deafness in children (Arch Otolaryng 43 473, 1946 Abst in Radiology 48 317, 1947) During the past three years, a total of 1,110 radium treatments have been given, using the Monel metal applicator designed by Crowe and Burnam, for the elimination of adenoids in 400 patients. Seventy-six patients received only a single radium treatment, 1 patient had nine treatments, and 1 has had ten treatments. The average period of observation for the total of 400 was thirteen months at the time of the report, and most of the interesting cases had been followed for almost two years. These patients received in addition to radiation therapy, surgical treatment of the tonsils or adenoids when indicated (mastoidectomy or nasal operation in some instances), and local treatments to the sinuses, the nose, or the ears. The treatment in many cases is not yet completed and the results should not be considered final. They are taken up under two headings: (1) changes in the nasopharyngeal lymphoid tissue, (2) changes in symptoms. At the last examination 99 patients had no lymphoid tissue in the nasopharynx and in an additional 167 patients only minute traces remained. At the first examination, 127 patients had a large mass of adenoid tissue, and 7 patients still had a large mass when last seen. At the first examination, 29 patients had normal eustachian orifices, and at the last examination 255 had normal eustachian orifices. Seventy-one surgical removals of lymphoid tissue were carried out on the 400 patients during the period of observation.

Audiometer tests were performed two or more times on 542 ears during this period. On the first test, 119 ears were normal in 280 hearing was slightly impaired, in 111 moderately impaired, and in 32 severely impaired. At the last test the hearing of 234 ears remained unchanged (101 of these normal on the first test), the hearing of 284 had improved and in only 24 had the hearing grown worse. Twelve of 33 chronically discharging ears healed completely during the period of observation, 9 became dry though perforations persisted, and 12 continued to discharge. Of 178 patients subject to unusually frequent and severe acute infections of the upper respiratory tract, 113 stopped catching colds completely or had few mild colds. Of 19 patients with bronchial asthma 9 no longer had attacks, and 5 others were greatly improved.

X-ray Irradiation to Promote Ovulation John O Haman West J Surg 55 107-111 February 1947

The author advocates treatment of amenorrhea with small doses of x rays over the ovaries and over the pituitary. The dosage to the pelvis varied from 225 r to 300 r with a similar dose over the pituitary. Treatments were given once weekly. Of the 32 patients treated ovulation was restored in 23. However careful scrutiny of the article reveals that some of these patients received thyroid extract and others estrogens. In one patient out of the series a permanent amenorrhea developed. Of 18 presumably sterile women, 60 per cent became pregnant.

[Results of the above treatment would seem encouraging but they are open to question on two scores. (1) The small number of cases reviewed. In

some of these women there might have been a return of menstruation without treatment. (2) Since both the pituitary gland and the ovaries were treated by radiation, it is not possible to tell which gland was the more responsible for the resumption of ovulation. Until more definite proof of the stimulating effect of radiation can be obtained at the hands of several observers, these treatments should not be generally recommended.—R C P.]

ROBERT C PENDERGRASS, M D

Functional Uterine Bleeding M Edward Davis M Clin North America 31 223-235, January 1947

Abnormal uterine bleeding is the most frequent gynecologic complaint. The term functional is applied to this bleeding when no organic disease of the reproductive organs is found. The bleeding is not in the normal pattern, and it can consist of an increased flow or a prolongation of the bleeding period (menorrhagia) or a complete irregularity of the menstrual pattern (metrorrhagia). The author takes up the causes and treatment of functional bleeding during adolescence, during the childbearing period, and at the menopause. It is with the patients in the last group that the radiologist is particularly concerned.

The treatment of bleeding at the climacteric involves several important principles. The possibility of cancer must be ruled out by careful examination—visualization of the cervix and biopsy of any questionable lesion, and a diagnostic curettage in the absence of gross disease. If cancer has been ruled out the onset of the amenorrhea of a natural menopause can be awaited unless the bleeding is considerable and troublesome. If, however, the bleeding should be stopped, some procedure leading to an artificial menopause should be adopted. Endocrine therapy must never be used for the control of functional bleeding at this time. Benign bleeding of the menopause can be treated by removal of the uterus by either an abdominal or vaginal hysterectomy, if there are no contraindications to surgery. In younger women this method is preferred to irradiation, since ovarian function can be saved. Many clinicians feel, however that in the menopausal period the ovaries have outlived their usefulness and remain as potential sites of neoplasms, particularly carcinoma, and that they should therefore be removed.

Irradiation controls functional bleeding in the menopausal period by destroying the remaining ovarian function. It is as effective as surgery in patients with normal pelvic organs, provided there is a proper selection of cases. The contraindications to irradiation in this selected group of cases are: (1) Uncertainty as to extent of the pathologic involvement. Whenever it is impossible to determine the exact state of the pelvic organs surgery is preferable to radiation. (2) Inflammatory conditions of the reproductive tract particularly the adnexa contraindicate irradiation. (3) Previous pelvic surgery. (4) Radiophobia. X ray radium and cancer are so closely associated in the minds of many patients that the use of radiation for the control of bleeding may be followed by undesirable mental reactions. Such patients are best treated by surgery.

If deep roentgen therapy is used the amount of irradiation which has been found effective in a large group of patients should be given. In most cases 400 r to each ovary will produce a permanent cessation of function.

The author's method for applying radium for castra-

tailed consideration of treatment technique, is intended mostly as a summary. The author states at the outset that 50 per cent of the cases he dealt with were in operable when first seen.

Tables are compiled showing the extent of involvement and the recovery rate in the favorable cases. The best group seems to be the one treated by operation followed by radiotherapy. No cases are tabulated in which surgery alone was employed, though this group should be of interest.

The author believes firmly in preoperative irradiation. The protagonists of this school of thought are diminishing in this country, probably faster than they are in France, where the idea of radiation has a more tenacious hold, possibly as a long shadow cast by the Curie Institute. When the radiologist has the upper hand in a clinic, preoperative irradiation is apt to be the rule, if the surgeon has the authority, preoperative irradiation is invariably conspicuous by its absence. Actually, if radiation has any place in the treatment of carcinoma of the rectum, it is as a palliative measure, either with or without operation, it seems to retard somewhat the more painful and otherwise distressing features of the terminal stages and serves a psychological value in giving the patient's relatives something on which to pin their flagging hopes.

PERCI J DELANO M D

Carcinoma of the Anus. Orville N Meland. *Am J Roentgenol* 57: 199-202, February 1947.

Meland previously reported (*Am J Roentgenol* 43: 706, 1940) on a series of 13 patients with squamous-cell carcinoma of the anus treated by irradiation alone. He now presents a follow-up on these patients along with information on 12 additional patients. He concludes that this form of therapy gives a reasonable hope for complete recovery with added hope of sphincter control. While some patients have some atresia of the anus, this is not enough to seriously inconvenience them. Even with this disability they are better off than the patients with a colostomy. It is felt that external irradiation when successful in destroying the disease, usually results in less sphincter disability than interstitial irradiation. Metastases in the uncontrolled cases involved the retroperitoneal nodes, liver and brain, rather than the groin.

ELLWOOD W GODFREY M D

Primary Malignant Tumours of Bone. Symposium. Stanford Cade, R W Scarff, F Campbell, Golding and S Bryan Adams. *Brit J Radiol* 20: 10-30, January 1947.

Cade points out that most malignant bone tumors fall into five classes: osteogenic sarcoma, Ewing's tumor, multiple myeloma, parosteal sarcoma, and osteoclastoma (giant-cell tumor). The clinical differences in the various types are well presented in a table which permits easy comparison.

A history of trauma is frequent. Pain and tumor are the chief clinical features, pain always preceding swelling. The balance between osteogenesis and osteoporosis in any tumor depends in part on the type of tumor and also on differences in vascularity. "Sun ray" spicules and "onion peel" layer are not always diagnostic of sarcoma.

Metastasis occurs with all malignant bone tumors, most commonly to the lungs and the lymphatic system, the viscera and the skeletal system. Bone metastases are particularly frequent in Ewing's tumor.

Ewing's sarcoma is the most sensitive to radiation and parosteal sarcoma the least. Irradiation will cause regression in sensitive types but it is not permanent. The best results are obtained with a combination of irradiation and surgery.

Preoperative irradiation should always be given for osteogenic sarcoma. Even when this fails to arrest the tumor growth, it temporarily inhibits the activity of the tumor, though there is no evidence that the delay alters the patient's chances of survival. In some cases regression may be so great that amputation may be postponed.

Multiple myeloma does not lend itself to surgical treatment.

Parosteal sarcomas call for amputation, followed by irradiation of the stump.

Good results are obtained in osteoclastoma by both surgery and irradiation. Surgery should be resorted to in young children in moderate sized tumors where the bone destruction is small, in tumors of the digits, and in cases in which the tumor has extended to the neighboring joint. Irradiation is indicated in healthy adults, for inaccessible tumors and for large growths. The effects of radiation become apparent in six weeks and continue for eight to ten months. A combination of surgery and irradiation is usually not advisable.

Scarff discusses certain pathological and radiological aspects of bone tumors. The relation of trauma to etiology is still unsettled, though there is considerable evidence that trauma plays a part in causing sarcoma and angioendothelioma.

The histologic appearance is important in the diagnosis. No real evidence has yet been brought forward to show that biopsy increases the liability to metastasis.

An exhaustive classification of bone tumors is not possible with our present state of knowledge. The following broad classification is suggested: infiltrating chondroma, osteogenic sarcoma, extraperiosteal fibrosarcoma, medullary fibrosarcoma, myeloma, Ewing's tumor, angio-endothelioma and chordoma.

Since there is no correlation between the histologic appearance of osteogenic sarcoma and the prognosis, there is little point in dividing this group into subdivisions. *Medullary fibrosarcoma* should be recognized as distinct from periosteal sarcoma because the prognosis is better. *Infiltrating chondroma* starts as an apparently benign growth but frequently develops the character of a highly malignant osteogenic sarcoma. There is considerable confusion in the Ewing's tumor group. Many are really neuroblastomas. *Angioendothelioma* shows a great variety of histological structure. Differentiation from secondary hypernephroma and Ewing's tumor may be impossible.

Golding discusses the relationship of the radiologist and the pathologist to diagnosis. He feels that greater accuracy in diagnosis will result from more attention to histology and thorough correlation of the pathological and x-ray findings. Radiologic diagnosis alone is not accurate enough. This is particularly true in giant cell tumors, central osteolytic tumors and chondrosarcomas.

Adams discusses the sensitivity of osteogenic sarcoma to radiation, pointing out that there is great variation in response and great difficulty in evaluating results. Since the disease is so uniformly fatal, every method of treatment should be tried.

SYDNEY J HAWLEY M D

treatment, one lived in good condition for fourteen months, but died at twenty months, 2 died three months and eleven months, respectively, after treatment, the last having been inadequately treated. Of the patients with chronic myeloid leukemia, 2 are living one year or more and 2 have died at four months and a year, respectively. Of those with chronic lymphatic leukemia, 2 are living eight and ten months, respectively, after treatment, 1 died of myocarditis shortly after treatment began and the other died in three months. The last was in the terminal phase when treatment was started.

One of the patients with giant follicular lymphadenopathy died at five months, having received treatment for palliation only, the other is living for thirteen months with moderate improvement. In the case of Hodgkin's disease, only a tracer dose was given. The patient with acute lymphatic leukemia received dramatic relief from dyspnea produced by massive mediastinal node enlargement, but died in six weeks. The case of polycythemia vera showed marked improvement over a period of three months and the patient was living at the time of this report.

The dosage varied from 2,000 to 7,000 microcuries per series of injections. The spacing of injections varied somewhat according to the disease present. In many instances, radioactive phosphorus therapy was supplemented by deep x-ray therapy. The author concludes that some cases showed good response even when apparently resistant to deep roentgen therapy. The remissions in chronic leukemia were generally longer than those obtained by deep x-ray therapy.

BERNARD S. KALAYJIAN, M.D.

Effects of Radioactive Phosphorus (P^{32}) on Normal Tissues. A Histologic Study of the Changes Induced in the Organs of Patients with Malignant Lymphomas. William R. Platt. *Arch. Path.* 43: 1-14, January 1947.

Although much has been written about the distribution and deposition of P^{32} in the peripheral blood and body tissues of certain laboratory animals and individual patients, few reports have been made on the histologic changes induced by this type of beta particle radiation.

The author reports a microscopic study of tissues from 43 cases including leukemias, Hodgkin's disease, multiple myeloma, lymphosarcoma, melanoma, and Ewing's sarcoma. Patients with malignant lymphomas who had not been treated with any type of radiation were studied as controls. Grossly, the observable changes were minimal. The following changes, it was felt, could be attributed to the effects of P^{32} .

Brain. Of 11 cases examined a few showed retrogressive changes such as disappearance of Nissl granules, loss of nuclei, pyknosis of chromatin matter, swelling and chromatolysis. Some changes were occasionally noted in the small blood vessels and capillaries.

Skin. The epidermis and dermis showed pathological changes quite similar to those following direct irradiation. These ranged from extreme atrophy, disarrangement and disappearance of the basement membrane of epidermal cells to marked hyperkeratosis. None of the extreme telangiectatic changes associated with local application of roentgen rays could be demonstrated.

Esophagus. The stratified squamous epithelium covering the mucous membrane of the esophagus revealed the same type of response that was seen in other

epithelium-lined internal structures, that is, vacuolation and desquamation of the epithelial cells with edema of the submucosa and infiltrating abnormal blood cells.

Gastrointestinal Tract. The mucosal epithelial lining showed occasional foci of superficial ulceration. Overproduction of mucus by goblet cells, which were enlarged and increased in number, was occasionally seen in distorted glands. Multinucleated, atypical giant cells were seen between the acini and in the submucosal coat proper. The muscle fibers were the sites of hyaline degeneration, interstitial fibrosis, edema, vacuolation and atrophy.

Liver. Liver changes which could be attributed directly to P^{32} were minimal when compared with the more frequently observed alterations in hepatic cells resulting from the anoxia of the severe associated anemia and with the degenerative changes secondary to the leukemic cellular infiltration.

Bone Marrow. Myeloid hyperplasia was shown in 20 cases, lymphoid hyperplasia and infiltration with hypoplasia of the other formed elements in 2, hypoplasia of all the blood cells in 2, and diffuse necrosis and fibrosis of the medullary cavities of both flat and long bones in 18.

Lymph Nodes. There was complete destruction of pattern in practically all of the leukemic nodes examined. This was usually associated with infiltration of immature myeloid, monocytic, and lymphoid cells.

Spleen. None of the spleens studied was smaller than normal. The external capsular surface was usually thickened and grayish white. Microscopically there was masking of the normal pattern by the malignant cellular invasion. Occasional extramedullary hemopoietic foci were also seen. The alterations more closely related to P^{32} therapy are an increase in fibrous tissue involving the trabeculae and the sinusoidal and arteriolar walls, focal fibrinous necrosis and hyalinization of these structures, and an increase in the number of multinucleated giant cells.

Kidneys, Ureters, and Bladder. Because of the difficulty of distinguishing renal changes secondary to primary vascular disease and those due to beta radiation, only those 15 cases in which the patient was below forty years of age were considered. The most characteristic changes were thickening and fibrosis of the renal capsule and hyalinization and thickening of Bowman's capsule with only rare involvement of the basement membrane of the glomerular tuft. Also observed were hyperemia, swelling, vacuolation and desquamation of the epithelium of the tubules, especially the convoluted tubules. In the bladder there were varying degrees of hyperemia, occasional edema, desquamation of epithelial cells and increase in hyalinized connective tissue involving the mucosa, submucosa, and muscularis.

Endocrine System. In the *pituitary gland* there was a slight to moderate increase of connective tissue distributed between the acini. The greatest and most constant alteration in the *adrenals* was marked dissolution of cells and loss of cellular detail. There were no significant changes in the *thyroid* or *parathyroid*. In the *pancreas* there was moderate to marked interacinar and interlobular fibrosis with occasional hyaline changes in the collagen fibers.

Reproductive Organs. In 11 of 16 patients under forty, there were varying degrees of destruction of the germinal epithelium of the testes. In practically all

tion is illustrated. Two capsules are inserted in tandem, the upper one in the uterine cavity contains radium and the lower one in the cervical canal extending through the internal os is empty. The total amount of irradiation necessary to produce castration consistently is about 1 800 to 2 000 milligram hours. The duration of the application depends upon the amount of radium used. However in most instances no more than 50 to 100 mg. of radium are necessary.

Radium and Roentgen Therapy in the Treatment of Menopausal Uterine Bleeding Herbert E Schmitz and Janet L Towne. *Am J Obst & Gynec* 53: 199-204 February 1947.

The authors record the irradiation of a series of 412 women varying in age from forty to fifty-one years who manifested abnormal uterine bleeding. The bleeding in no case was due to a malignant growth as revealed by diagnostic curettage, which was performed in all cases prior to the institution of therapy. It should be noted, however, that 236 patients had small myomas, which in no case were larger than a three months' gestation.

Most of the cases were treated with intrafundal application of radium. In order to secure complete amenorrhea, 1,800 mg. element hours were necessary. A 2 mm. brass capsule containing 50 mg. of radium was inserted in the uterine cavity for thirty five hours. The remainder of the patients were successfully treated with external irradiation employing a tissue dosage of approximately 500 r delivered into the mid pelvis through two fields, one suprapubic and one sacral (200 kv., filtration of 0.5 to 1.0 mm. Cu plus 1.0 mm. of Al). It is concluded that in selected cases of benign uterine hemorrhage, irradiation should be employed rather than major surgery.

FRANCIS F HART, M D

Evaluation of the Surgical Treatment of Recurrent Echinococcal Cysts of the Liver Followed by Deep X-Ray Therapy G M Dorrance and J S Bransfield. *Am J Trop Med* 27: 77 January 1947.

In 1928 a patient was operated upon for echinococcal cyst of the liver. A recurrence, five years later involved about one-sixth of the liver substance. After removing a large number of daughter cysts and necrotic material the cyst was marsupialized by sewing the cut edges to the peritoneum. Six months after the operation daughter cysts were being extruded from the sinus. Over a twenty-day period, ten x ray treatments totaling 1,200 r were given over the anterior surface of the liver (200 kv. with a filter of 0.5 mm. Cu and 1 mm. Al) followed by nine treatments over the posterior surface for a total of 1 030 r. Two weeks following the second treatment no cysts were extruded from the sinus and a week later it had healed. Nine years later there was no evidence of recurrence.

Benign Giant Cell Tumor of Bone. Report of a Case Treated by X-Ray Radiation 5 Years ago Paterno S Chikiamco. *J Philippine M A* 23: 19-22 January 1947.

A case of giant-cell tumor involving the upper portion of the humerus and a part of the epiphyseal head was diagnosed roentgenologically in January 1940. The tumor responded promptly to deep x ray therapy (dosage not given), and a roentgenogram of the affected area in December 1945 shows the bone practically normal.

RADIOACTIVE ISOTOPES

Radioactive Phosphorus (P^{32}) and Alkylamines (Nitrogen Mustards) in the Treatment of Neoplastic and Allied Diseases of the Hemopoietic System. Leon O Jacobson, Charles L Spurr, T R Smith and G F Dick. *M Clin North America* 31: 3-18, January 1947.

Radiophosphorus and methyl bis (8-chloroethyl) amine hydrochloride (called Dema for the sake of brevity), like x-radiation, have definite limitations in the treatment of neoplastic diseases of the hemopoietic system. The course of the acute leukemias and multiple myeloma is unaffected by these agents. Radiophosphorus usually does not favorably influence the course of Hodgkin's disease, while Dema and roentgen therapy produce definite remissions. More or less comparable remissions are produced in chronic myelogenous leukemia by the administration of P^{32} and x radiation, while Dema produces only a short or wholly unsatisfactory clinical response. The three agents are roughly equivalent in therapeutic efficacy in lymphosarcoma. Radiophosphorus induces satisfactory remissions in polycythemia rubra vera with regularity. Observations on patients after treatment with Dema are not long nor extensive enough to permit a logical comparison with the results obtained with P^{32} . Dema has produced clinically significant remissions in the few patients thus far.

Radiophosphorus is effective in the diseases discussed when given orally or intravenously. If given by mouth, it should be administered in orange juice in the morning and breakfast omitted or postponed for at least two to three hours. A 75 per cent absorption should be assumed with oral administration. The effective and 'safe' dose or dosage schedule is highly individualized. The possible serious toxic reactions to the isotope are leukopenia, thrombocytopenia, and anemia.

The dose of Dema in the diseases in which a trial is indicated is usually 0.1 mg. per kilogram of body weight per day intravenously for four consecutive days. In individual cases a shorter or longer course of therapy may be indicated. The serious toxic manifestations of Dema which may ensue are (1) nausea and vomiting two to three hours after administration of the drug, (2) thrombophlebitis and thrombosis at the site of injection if the material is not sufficiently dilute when given intravenously and (3) leukopenia thrombocytopenia and anemia.

Four case histories are presented to illustrate the therapeutic effect and some toxic manifestations of P^{32} and Dema. References to the literature are included.

Preliminary Report on the Use of Radioactive Phosphorus in Australia A G S Cooper. *M J Australia* 1: 104-113 Jan 25 1947.

This paper covers the results of the treatment of 18 patients with radioactive phosphorus. There were 5 cases of lymphosarcoma, 4 of chronic myeloid leukemia, 4 of chronic lymphatic leukemia, 2 of giant follicular lymphadenopathy and 1 each of Hodgkin's disease, acute lymphatic leukemia and polycythemia vera.

The drug was given intravenously in all cases using a rapid fractional saturation method in most instances. Of the lymphosarcoma patients 2 are living in good condition three years and six months respectively after

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instances the seminiferous tubules showed thickening and varying degrees of hyalinization of the tunica propria and the basement membrane. The most conspicuous change in the ovaries was disappearance of the primary and graafian follicles.

Heart Minimal degenerative changes were observed in the myocardium and coronary blood vessels in 14 of 21 patients under forty years of age.

Lungs Pulmonary alterations ranged from moderate congestion, edema, lymphangiectasis, slight inflammatory cell infiltration and minimal degenerative metaplastic changes in bronchial and alveolar epithelium to well defined hyaline membrane formation, extreme thickening of alveolar walls, focal atelectasis and thickening of pulmonary vessels, with associated swelling of collagen and hyalin degenerative changes therein.

Bone In the bone there were disappearance of osteoblasts and absence of osteocytes and lacunae.

Skeletal Muscle Loss of cross striations, fragmentation of fibers, homogeneity of myoplasm, and nuclear karyorrhexis were characteristic changes in skeletal muscle.

Those tissues which utilize phosphorus rapidly and which also have a high phosphorus content, *i.e.*, bone marrow, liver, spleen, and lymph nodes, specifically take up higher concentrations of radioactive phosphorus than do normal tissues. Therefore, proportionately higher concentrations of radioactivity are formed in those tissues preferentially involved in malig-

nant lymphomas and primary polycythemia. Also it is noted that in almost every therapeutic application of radiation, normal tissues are affected as well as the intentionally radiated focus of disease. The effect on the bone marrow has led to variable hematologic complications. When two or more of the cellular elements of the marrow were depressed in the same patient the formed elements of the peripheral blood showed changes in the following order: The leukocyte level decreased first, the thrombocyte level second and the erythrocyte level last. The most prominent alterations in immature marrow cells were in the megakaryocytes which were degenerated or absent in most of the marrow sections studied. Therefore on the basis of clinical and pathological studies, reaction to P^{32} in order of decreasing cellular sensitivity should be leukocytes and leukopoietic tissue, megakaryocytic tissue, and lastly erythropoietic tissue.

The urinary excretion of P^{32} varies from 5 to 25 percent during the first four to six days in patients with leukemia and polycythemia vera, but 25 to 50 percent is excreted by normal subjects in the same period. The difference is attributed to quick fixation of P^{32} in pathologic tissues and cells. The resultant prolonged irradiation of the renal parenchyma could result in nephritis and hypertension.

Serious consideration should be given to the changes in the testes and ovaries of patients in the reproductive period of life.

PAUL W. ROMAN, M.D.

EXPERIMENTAL STUDIES

Pituitary-Adrenal Cortical Control of Lymphocyte Structure and Function as Revealed by Experimental X-Radiation. Thomas F. Dougherty and Abraham White. *Endocrinology* 39: 370-385, December 1946.

CBA mice 60 to 80 days old were given total body x radiation. A large dose 200 r produced within three hours a lymphopenia, tissue lymphocyte degeneration, and total serum protein and gamma globulin increases. These changes also occurred in adrenalectomized mice receiving 200 r one day after operation. This dose gave an anamnestic response (*i.e.* enhancement of antibody titer) in previously immunized mice in the absence of the adrenals.

It was demonstrated that 10 r produced the same physiological alterations, including the anamnestic response, in normal but not in adrenalectomized mice. Therefore, 10 r influenced lymphoid tissue function by augmenting pituitary-adrenal cortical secretion. Large doses of x radiation may produce lymphocyte degeneration without adrenal mediation and thus increase circulating gamma globulin and antibodies. This is further proof that adrenal cortical steroids produce hyperglobulinemia by their degenerative effects on the lymphocyte, an end cell of adrenal cortical hormone action.

It is suggested that x-rays exert both a direct and an indirect effect on lymphocytes. The direct action may be manifested even in the absence of pituitary or

adrenals, whereas the indirect action is mediated through the pituitary-adrenal cortical mechanism.

The Conjugate Role of Trauma and of a Radioactive "Soil" in the Production of Experimental Osteosarcoma. G. Gincouff and H. Fajerman. *Atomes et radiations* 1: 32-37, November-December 1946.

The authors have carried out carefully controlled experimental work in which a number of laboratory animals were given intensive radiation, sometimes by radium implantation and sometimes by intravenous injections of radioactive salts and were then under anesthesia, made the subjects of fractures of various bones. The healing fractures were followed with films for varying periods and the dates at which identifiable sarcomas of bone appeared at the fracture sites were recorded. Some tumors were seen as early as five months after the fracture, others a year or more later. In most of the cases metastases were widespread. In some instances where no sarcoma developed the fracture callus was huge out of all proportion to that ordinarily found in simple fracture.

One cannot but conclude after surveying these experiments that any amount of radioactive material introduced into the body must carry with it a certain hazard.

PERCY J. DELANO, M.D.

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